ASSOCIATION OF DIETARY SODIUM AND POTASSIUM WITH BLOOD PRESSURE IN A TERTIARY CARE CENTRE

Dissertation

Submitted to

THE TAMILNADU Dr. M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the requirements for the award of the degree of

M.D. GENERAL MEDICINE

BRANCH I

OCTOBER 2017

CERTIFICATE

This is to certify that this dissertation entitled **"Association of dietary sodium and potassium with blood pressure in a tertiary care centre"** is a bonafide record of the work done by **Dr. Shahbaz Zailu Mohamed** under guidance and supervision in the Department of General Medicine during the period of his postgraduate study for **M.D General Medicine [Branch-I]** from 2014 to 2017.

Dr. R Mohandhas

[Guide]

Professor
Department of General Medicine
Sree Mookambika Institute of
Medical Sciences,
Kulasekharam, Kanyakumari,
Tamil Nadu -629 161

Dr. V Rajendran

[Co-Guide]

Professor
Department of General Medicine
Sree Mookambika Institute of
Medical Sciences,
Kulasekharam, Kanyakumari,
Tamil Nadu -629 161

Dr. J. KANIRAJ PETER

Professor & Head of Department
Department of General Medicine
Sree Mookambika Institute of Medical Sciences,
Kulasekharam, Kanyakumari,
Tamil Nadu -629 161

Dr. REMA V. NAIR

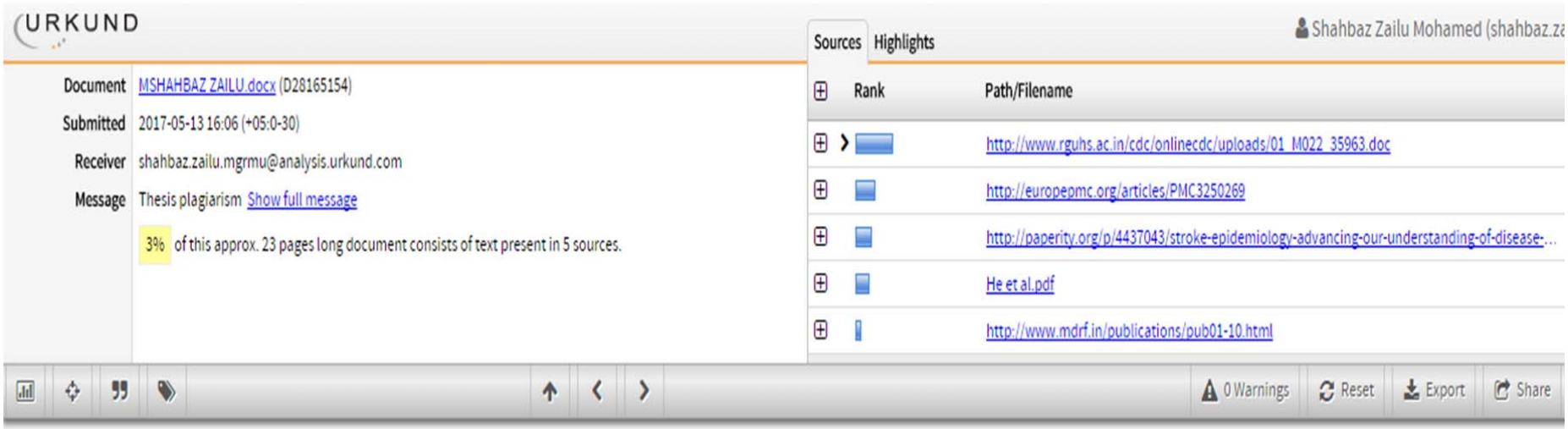
Director,
Sree Mookambika Institute of Medical
Sciences,
Kulasekharam
Kanyakumari
Tamil Nadu -629 161

DECLARATION

I solemnly declare that this dissertation **"Association of dietary sodium and potassium with blood pressure in a tertiary care centre"** was prepared by me at Sree Mookambika Institute of Medical Sciences, Kulasekharam - 629161 under the guidance and supervision of **Dr. R. MOHANDHAS** , Professor of General Medicine and **Dr. V. RAJENDRAN ,** Professor of General Medicine , Sree Mookambika Institute of Medical Sciences, Kulsekharam. This thesis is submitted to the Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of MD Degree examination in General Medicine.

Dr. Shahbaz Zailu Mohamed

Junior Resident
Department of General Medicine,
Sree Mookambika Institute of Medical Sciences,
Kulasekharam
Kanyakumari
Tamil Nadu -629 161



ASSOCIATION OF DIETARY SODIUM AND POTASSIUM WITH BLOOD PRESSURE IN A TERTIARY CARE CENTRE

Dissertation

Submitted to

THE TAMILNADU Dr. M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the requirements for

the award of the degree of M.D. GENERAL MEDICINE

BRANCH I OCTOBER 2017

INTRODUCTION With the changing life style and increasing daily stress the incidence of hypertension is on the rise . Hypertension is considered as the number one silent killer among all the diseases worldwide. Hypertension remains to impose burden to the society in terms of an enormous health and economic expenditure although there are wide variety of drugs to combat hypertension.

It is an interesting fact that not only is hypertension on the rise but also the prevalence of uncontrolled hypertension is continuously rising all over the world. This points towards the fact that there is an important

ACKNOWLEDGEMENT

I thank **God** Almighty, for all blessings without which this work would not have been possible.

I express my heartfelt gratitude to our Director Dr. Rema V. Nair and our Chairman Dr. C.K.Velayuthan Nair for providing me the facilities required and for permitting me to carry out the study in this institution.

I would like to thank our principal Dr. Padmakumar for being supportive of the study till the very end.

I thank my HOD Dr. J. Kaniraj Peter, for the creative suggestions, timely advice and constant encouragement. It has been a wonderful experience to work under his guidance.

I thank my guide Dr. R. Mohandhas and co-guide Dr. V. Rajendran for their valuable help, suggestions and supervision throughout the study. They lent their full support in times of difficulties that I encountered during this study period without which this dissertation would not have been completed on time. Their encouragement from the beginning of this research to its completion has been profound.

I humbly thank Dr. Mookambika R.V. our Academic Co-ordinator and Vice-principal whose support and guidance kept me in full swing throughout my study period. Her suggestions were very valuable at each stage of my

dissertation work. I am indebted to her for the guidance and support throughout my post graduate days.

I would also like to thank Dr. Vinu Gopinath, our Medical Superintendent whose guidance and help were crucial to this study.

I am grateful to Dr. Thilagar and Dr.Krishnankutty for their valuable support and constant encouragement.

I thank Dr.Ajay Kumar, Dr. Sheeba George, Dr. Kiron Sukulal, Dr. Beena Unnikrishnan and Dr.Reneega Gangadhar for their valuable guidance.

I also extend my sincere thanks to Dr. Sanjeeva Gowda, Dr. Rufus Demel, Dr.Sreetha Sreenivas , Dr.Aiswarya Dhanapalan and all the staff members of Department of General Medicine for their support.

Sincere thanks to Dr. Prashanth Solanke and Jossy for all their help concerning my issues with statistics.

I am grateful to my colleagues, Dr.Jayaram J. K., Dr.Jaison Varghese, Dr.Jineesh Raj, Dr. Jacob C Pilla, Dr. Aswathi Harikumar, Dr. Arun M.A and Dr. Bijo K Benny for their support in various technical aspects of my study.

I am grateful to my all family members who supported me a lot and have always encouraged me to do better.

Without the whole hearted cooperation of my patients, this thesis would not have reached a conclusion. I express my sincere gratitude to all my patients at Sree Mookambika Institute of Medical Sciences, Kulasekharam.

Dr. Shahbaz Zailu M

ABSTRACT

BACKGROUND AND OBJECTIVES

Hypertension is a leading cause for Non Communicable diseases.The aim was to study the association of dietary sodium and potassium as estimated from the urinary excretion of these cations with blood pressure.

METHODS

Institutional Human Ethical committee clearance was obtained. After taking an informed consent, 260 patients were enrolled in the study which included 130 hypertensives and 130 non-hypertensives. All the subjects were in the age group of 30 to 79 years. A random clean catch urine sample was collected for estimation of sodium and potassium and routine blood tests for hypertension workup were done.The 24 hour urine sodium and potassium was estimated from the spot samples using the Kawasaki formula. Data collected was analysed by SPSS version 20.1

RESULTS

The average systolic BP among the non-hypertensives was 117.6 ± 9.05 and average diastolic blood pressure was 72.15 ± 6.93. The average systolic blood pressure among the hypertensives was 143.3 ± 15.1 and average diastolic blood pressure was 90.92 ± 7.41. The average urinary sodium excretion in 24 hrs among non- hypertensives was 5131.49 ± 1013.65 mg/d and among hypertensives was 6343.05 ± 2362.73 mg/d. The average

urinary potassium excretion in 24 hrs among the non-hypertensives was 2100.72 ± 476.47 mg/d and among hypertensives was 2291.61 ± 534.93 mg/d. The mean ratio of 24 hr urinary excretion of sodium to 24 hr urinary excretion of potassium was 2.51 ± 0.55 in the non-hypertensive group and 2.72 ± 0.59 mg/d in the hypertensive group.

There was a positive correlation between the daily urinary sodium, urine potassium and 24 hr urine sodium-potassium ratio with systolic and diastolic BP among the hypertensives. There was no significant correlation among the non-hypertensives.

CONCLUSIONS

In a developing country like India to control the menace of hypertension, modifiable risk factors like dietary salt intake need to be controlled. Government policy makers and NGOs should work together to conduct salt reduction programmes to create awareness among the public and avert premature death and disability.

Key words: Hypertension, Urinary sodium, Urinary potassium

LIST OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF GRAPH

INTRODUCTION

With the changing life style and increasing daily stress the incidence of hypertension is on the rise. Hypertension is considered as the number one silent killer among all the diseases worldwide. Hypertension remains to impose burden on the society in terms of an enormous health and economic expenditure although there are wide variety of anti-hypertensives to combat it. It is an interesting fact that not only is hypertension on the rise but also the prevalence of uncontrolled hypertension is continuously rising all over the world. This points to the fact that there is an important need to understand the underlying mechanism's of hypertension, more importantly the modifiable risk factors and intervenable risk factors.[1]

The World Health Statistics in the year 2012 estimated that there were fifty seven million global deaths in 2008, sixty three percent of them were due to diseases that are non-communicable diseases. The largest proportion of non-communicable disease deaths is caused by cardiovascular diseases (48%). In terms of attributable deaths, elevated blood pressure level plays a significant role as a behavioral and physiological risk factor for 13% of the global deaths. Hypertension is the fourth contributor to premature death in developed countries and the seventh in developing countries.[2,3]

Hypertension in adults ≥ 18 years is defined as systolic blood pressure (SBP) of ≥140 mm Hg and/ or diastolic blood pressure (DBP) of ≥90 mm Hg or any level of blood pressure in patients taking medication for hypertension.[1,4]

Untreated or poorly controlled hypertension leads to target-organ damage (TOD) and its serious vascular complications events like hypertensive nephropathy, hypertensive cardio-myopathy, heart failure, myocardial infarction, cerebro-vascular accident, hypertensive retinopathy, atherosclerosis, aneurysms and cardiovascular disease which drastically decreases the life expectancy, quality and productivity of the individual.

Inspite of all these well-known complications of uncontrolled hypertension it remains inadequately detected and treated. This is mainly due to the asymptomatic nature of the disease, especially during the initial years while there is an ongoing damage to multiple organ systems. Hence cardiovascular risk and its complications remains high among hypertensive patients.

Studies have demonstrated that there exists a continuous relationship between the blood pressure levels and the probable risk of developing complications. The risk of developing cardiovascular complications starts at 115/75 mmHg and is seen to double with each increment of 20/10 mm Hg throughout the blood pressure range.[5-7] For persons over the age of 50 years, Systolic blood pressure is seen to be a more important risk factor of CVD than Diastolic blood pressure and moreover Systolic Bp is more difficult to control than Diastolic Bp in this population. Recent studies point to the fact that the risk of developing cardiovascular events in Asian Indians is higher at relatively lower levels of blood pressure when compared to the Western population.

Multiple international authorities have come forth with various definitions of hypertension which are all arbitrary. The term 'Pre-hypertension'

coined by the Joint National Committee VII guidelines includes a wide range of BP from normal to high normal taking into fact that there is a strong evidence that this high normal population needs to be treated sometimes, especially in the presence of co- morbidities like diabetes mellitus or a family history of hypertension.[4,8]

A review of epidemiological studies in India suggests that the prevalence of hypertension has increased from 2% to 25% among the urban population and from 2% to 15% among the rural population in the last six decades. In a meta-analysis of multiple cardiovascular epidemiological studies carried out in our country, it was seen that prevalence rates of coronary artery disease and stroke have raised more than thrice in the Indian population. In the INTERHEART and INTERSTROKE study, hypertension accounted for 17.9% and 34.6% of population attributable risk of various cardiovascular risk factors for coronary artery disease and stroke respectively. According to the Indian Ministry of Health and Family Welfare, the overall prevalence of hypertension in India by 2020 will be 159.46/1000 population.[9,10]

Multiple factors might have contributed to this increasing trend, attributable to various indicators of economic progress such as increase in the life expectancy, urbanization and its attendant lifestyle changes including increase in salt intake in the form of tinned foods and cola and the overall epidemiologic transition. The prevalence of hypertension has seen to increase with age among all populations. There is a marked increase in the prevalence of

diabetes, dyslipidemia, metabolic syndrome and obesity while that of smoking has declined.[10-12]

In a developing country like India hypertension awareness, treatment and control status is low, with only half of the urban and a quarter of the rural hypertensives actually being even aware that they have the disease. Inspite of all the awareness programmes being conducted by the Government it is seen that only one in five persons is actually on treatment among which less than 5% have their blood pressure under control. With more than enough evidence showing the deleterious effects of a sustained uncontrolled blood pressure on the population, more aggressive preventive measures are required so as to reduce obesity, increase the physical activity, decrease the salt intake of the population and a collective effort to promote awareness about hypertension and its other related risk behaviours.

Effective population-based interventions are necessary to control the global burden of cardiovascular disease. Reducing dietary salt intake has emerged as a primary goal, with many guidelines including the World Heart Organization (WHO) in 2003, recommending that the adult population ingest <2.0 g/day of sodium (which corresponds to 5 g of salt/day), based on epidemiological studies which indicated a linear association between increasing levels of sodium intake and cardiovascular events[13] and clinical trials that showed that a lower level of dietary sodium intake was associated with significant reduction in blood pressure.[14-16]

Since then, however, there have been a number of clinical trials and studies that have questioned whether this recommendation for dietary sodium intake is optimal, with some recent prospective cohort studies indicating that a sodium intake of under 3 g/day (the current guidelines recommendation) may be actually deleterious and associated with an increased risk of cardiovascular death.[17-20]

These newer studies, and the fact that there are no definitive randomized controlled trials which show that reducing dietary sodium intake to low levels will reduce cardiovascular morbidity and mortality, have re-ignited the controversy surrounding the optimal target for sodium intake among the scientific fraternity. Since 1980s many research's have been published regarding the association between dietary sodium intake and blood pressure and cardiovascular disease and till date there are very few areas in CVD prevention that evoke more diverse opinions.

Diet being a modifiable factor plays a very important role in the etio-pathogenesis and the treatment of hypertension. The dietary factors responsible for hypertension revolve around the electrolytes sodium and potassium. Hence I conducted the present study entitled "Association of dietary sodium and potassium with blood pressure in a tertiary care centre" to better understand the association of dietary intake of sodium and potassium with blood pressure.

AIMS AND OBJECTIVES

- To study the association of dietary intake of sodium and potassium as estimated from the urinary excretion of these cations with blood pressure.
- To study factors associated with dietary intake of sodium and potassium in the hypertensive group and normal population.

HYPOTHESIS AND SCIENTIFIC JUSTIFICATION

HYPOTHESIS

The alternate hypothesis states that there is a statistically significant association between dietary intake of sodium and potassium with blood pressure among the hypertensives.

SCIENTIFIC JUSTIFICATION

In this era of modern medicine, Non-Communicable Diseases (NCD) form the major cause of morbidity and mortality. The largest proportion of NCD deaths is caused by cardiovascular diseases. Over the years, epidemiological studies and clinical trials have shown a continuous linear relationship between high sodium intake and the risk of cardiovascular disease. These results are yet insufficient to conclude whether low sodium intake is associated with an increased or reduced risk of cardiovascular disease in the general population.

Recently, few studies have also shown that a low salt intake may be associated with adverse health effects in some subgroups, including some patients with heart failure or other forms of cardiovascular disease, diabetes, or chronic kidney disease. Thus, there are inconsistencies whether a low sodium diet decreases the cardiovascular risk among the normal population and hypertensives or in the contrary is actually deleterious.

Then, there is the concept of salt sensitivity wherein blood pressure of some members of the population (salt-sensitive SS) exhibit changes parallel to changes in salt intake whereas the salt resistant (SR) ones do not.

The association of dietary sodium and potassium with blood pressure is thus a very interesting and controversial topic. There are few studies from Chennai regarding the subject. The dietary intake of sodium and potassium and its association with blood pressure and other parameters among the population visiting our tertiary care centre SMIMS, Kulasekharam located in South Tamil Nadu would make a good study.

In this dissertation, I have proposed to estimate the dietary intake of sodium and potassium from the urinary excretion of these cations and compare it with the blood pressure of normotensives and hypertensives .

REVIEW OF LITERATURE

EPIDEMOLOGICAL TRENDS IN HYPERTENSION

Definitions

Hypertension as per the World Health Organization is defined as " a rise in blood pressure (Systolic above 140 and Diastolic above 90 mm Hg) or taking antihypertensive medication."[13]

Blood pressure is defined as a continuous variable with no absolutely dividing line between normal and abnormal values. The best operational definition is "the level at which the benefits (minus the risks & costs) of action exceeds the risks and costs (minus benefits) of inaction." [22]

The definition of hypertension for home & ambulatory blood pressure monitoring (ABPM) is different: [44]

Mean 24-hr ABPM SBP ≥130 mm Hg or DBP ≥80 mm Hg or

Mean awake SBP ≥135 mmHg and /or DBP≥85 mm Hg

EPIDEMIOLOGY OF HYPERTENSION

It has been foretold that the global prevalence of hypertension would rise in the twenty years by more than two fold from around 26% in 2005 to 60% by 2025. [24]

Studies from various countries show an increasing prevalence of hypertension, the possibility being the fact that the changing lifestyle pattern including dietary habits, urbanisation, the aging population, increasing body mass index, stress and sedentary lifestyle all which lead to the development of hypertension. [25-26]

WORLD HEALTH ORGANIZATION CLASSIFICATION OF HYPERTENSION

The WHO/ISH blood pressure classification includes 3 grades of hypertension. Each stage of hypertension is characterized by the presence or absence of markers of hypertensive cardiovascular disease and the evidence of target organ damage irrespective of the blood pressure level.

CATEGORY	SYSTOLIC (mmHg)	DIASTOLIC (mmHG)
Optimal	<120	<80
Normal	<130	<85
Grade 1	140-159	> 90-99
Grade 2 Hypertension	160-179	>100-109
Grade 3 Hypertension ("severe")	>180	>110
Isolated Systolic Hypertension	>140	<90

FIGURE 01 : The WHO/ISH blood pressure classification

Definition must be flexible taking into account CV risk profile

Other risk factors and disease history	Blood pressure (mmHg) Normal SBP 120–129 or DBP 80–84	High–normal SBP 130–139 or DBP 85–89	Grade 1 SBP 140–159 or DBP 90–99	Grade 2 SBP 160–179 or DBP 100–109	Grade 3 SBP >180 or DBP >110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1–2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors or TOD or diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
ACC	High added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

TOD – Target Organ Damage ACC - Accompanying Clinical Conditions

FIGURE- 02 : CV risk stratification according to BP, other risk factors and disease history

The ESH-ESC guidelines recommend a target bp of < 140/90 mmHg for patients with uncomplicated hypertension as this is associated with average CV risk according to the Framingham study. [48]

Classification	Normal	Stage 1 hypertension	Stage 2 hypertension	Stage 3 hypertension
Descriptive Category	Normal BP or rare blood pressure elevations **AND** No identifiable CVD†	Occasional or intermittent BP elevations **OR** Early CVD†	Sustained BP elevations **OR** Progressive CVD†	Marked and sustained BP elevations **OR** Advanced CVD†
Cardiovascular Risk Factors	None or few	Several	Many	Many
Early Disease Markers	None	Usually present	Overtly present	Overtly present with progression
Target-organ Disease	None	None	Early signs present	Overtly present with or without CVD events

FIGURE--03 : ASH Writing Group definition and classification of hypertension

The Amercan Society for Hypertension in the article Dietary Approaches to lower Blood pressure states that the risk factors for elevated blood pressure include increased salt intake, a low potassium intake, overweight, alcohol abuse, and sub-optimal dietary patterns. The efforts to decrease blood pressure should be carried out not only in the hypertensives but also the non-hypertensives as studies have shown that dietary and lifestyle modifications prevent and delay if not stop the occurrence of hypertension. [49]

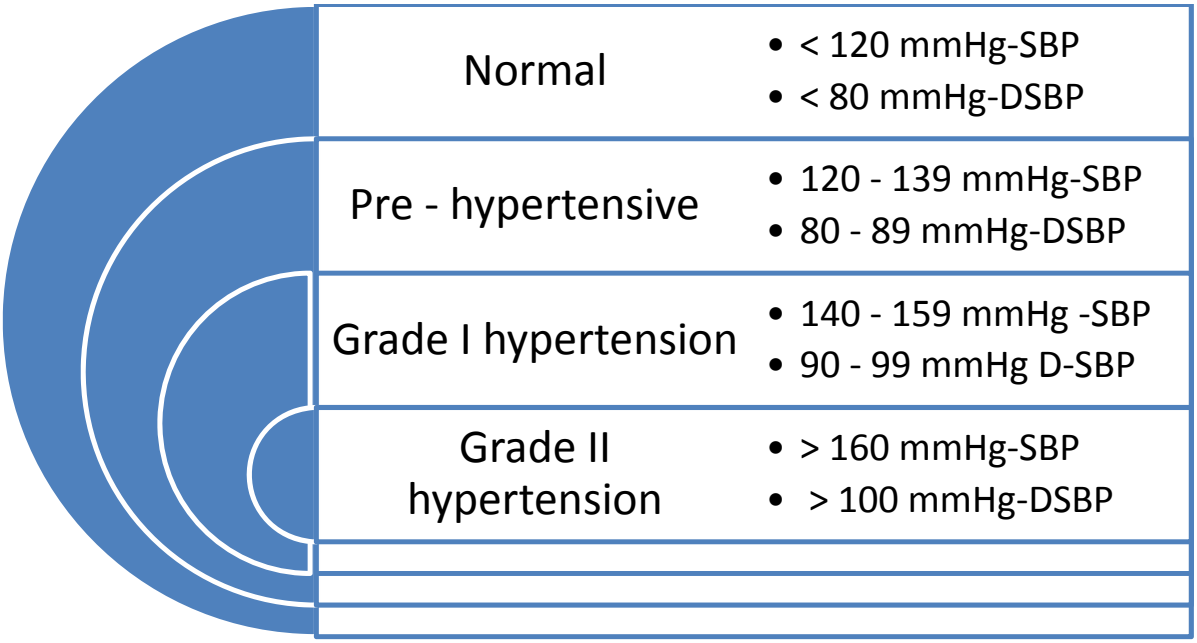


FIGURE 04: JNC VII1 Classification of Hypertension [44]

PATIENT SUBGROUP	TARGET SBP (mm Hg)	TARGET DBP (mm Hg)
≥ 60 YEARS	< 150	< 90
< 60 YEARS	< 140	< 90
> 18 YEARS WITH CKD	< 140	< 90
> 18 YEARS WITH DM	< 140	< 90

TABLE 01 : JNC VIII Target BP Recommendation [44]

Group	BP Goal (mm Hg)		
	General	DM*	CKD**
JNC 8:	<60 yr: <140/90	< 140/90	< 140/90
	≥60 yr: <150/90		
ESH/ESC:	< 140/90	< 140/85	< 140/90
Elderly	140-150/90	(SBP < 130 if proteinuria)	
	(<80 yr: SBP<140)		
ASH/ISH	< 140/90	< 140/90	< 140/90
	≥80 yr: <150/90	(Consider < 130/80 if proteinuria)	
AHA/ACC	< 140/90	< 140/90	< 140/90

FIGURE 05: Comparison of recent guideline statements

* **ADA ≤ 140/80 mm Hg**

** **CDA < 130/80 mm Hg**

The "Rule of Halves"

Hypertension remains an "iceberg" disease, with a significant percentage of cases being undetected. In the early 1970's studies showed that only half of the hypertensive population in developed countries were aware of the condition. Among them, only about half of them were under treatment, and only half of those being treated had optimally controlled blood pressure. This came to be known as the "rule of halves" and it is the present scenario in the developing countries.

Natural history of untreated HT

In untreated hypertensive cases as the age progresses there is a steady rise in the systolic blood pressure and a decline in the diastolic blood pressure .Thus in adults above the age of 50 years hypertension has a linear association with systolic blood pressure than with diastolic blood pressure.

Hypertension is a major risk factor for ischemic heart disease, strokes, cardiac failure, renal failure , decreased cognitive capabilities and all-cause mortality. The degree of decrease in blood pressure is associated in a linear fashion with risk reduction.[5]

Pre hypertension is related with double the risk of developing cardiovascular and cerebro vascular complications in women when compared to non hypertensive women.

The prevalence of hypertension is higher in men until the age of 45 years, in the age group of 45 years to 64 years the prevalence rate is equal and above the age of 64 years the prevalence is more in women. [1,2]

The awareness regarding this silent pandemic and the treatment rates have substantially increased over the years. But data show that even among the known hypertensives about 50% do not have controlled blood pressures. [44] This data is more significant among adults greater than 80 years.

Risk Factors

Risk factors for hypertension are as classified as modifiable and non-modifiable risk factors

Modifiable Lifestyle Risk Factors

Cigarette Smoking

Promotes s hypertension by the following factors

- Reduced blood vessel compliance,
- Increased fibrinogen levels,
- Increased platelet aggregation,
- Decreased high-density lipoprotein cholesterol levels,
- Higher hematocrit

Active cigarette smoking is the cause for around 18% of cerebrovascular accidents worldwide. Even passive cigarette smoking is shown to cause accelerated atherosclerosis.

Alcohol Consumption

Heavy alcohol consumption favors hypertension complications by

- Elevating blood pressure,
- Increasing the coagulability,
- Predisposing to cardiac arrhythmias
- Decreasing the cerebral blood flow

Sedentary life style

Increased physical activity reduces the pro-athrogenic factors. A meta-analysis of 23 studies that examined the relationship of physical activity with risk of developing stroke noted that highly active subjects experienced a 27% lower risk of stroke or mortality when compared to low-active subjects.

Diet

Clinical trials have proven for years that adopting a low-risk diet accompanied by optimal weight reduction especially in the society would drastically decrease the burden of hypertension.

JNC VIII recommends a limited sodium intake with adequate calcium and potassium in the daily diet. It also recommended the Dietary Approaches to Stop Hypertension (DASH) dietary model with lower content of total fat and saturated fat and plenty of low-fat dairy products, fruits and nuts and vegetables.

Non-Modfiable Risk Factors

Age

Age is a very important non modifiable risk factor for development of hypertension. In a developing country like India, the complications of hypertension like stroke is seen to occur at a younger age than other countries. The average age of patients with stroke is 15 years younger than those in the developed countries. Around 20% of patients admitted with cerebro vascular accidents in India are aged less than 40 years. [10]

Gender

Males are more prone for development of hypertension than females. The prevalence of hypertension is higher in men until the age of 45 years and in the age group of 45 to 64 years, the prevalence rate is equal and above the age of 64 years the prevalence is more in women.

Race and ethnicity

Disparities in the level of blood pressure with race and ethnicity persist. The prevalence of hypertension is higher among the blacks than the whites and the blacks have been found to have higher average blood pressure measurements than the whites.[7] This has also reflected in the incidence of complications with the blacks developing 1.8 times more strokes, 1.5 times more cardiovascular complications and 4.2 times more kidney disease when compared to the white population.

Heredity

Among individuals with a family history of hypertension, its incidence occurs 3.8 times more frequently before the age of 55.

Genetic Factors

Genes encoding for renin–angiotensin-aldosterone system with polymorphisms of angiotensinogen and angiotensin–converting enzyme are postulated to be associated with hypertension and the individual's blood pressure response to dietary salt intake. The alpha-adducin gene is responsible for the higher renal tubular absorption of sodium and genetic variations are postulated to cause hypertension.

THE ROLE OF SODIUM AND POTASSIUM IN HYPERTENSION

Epidemiological Back Ground

There is strong evidence that exists a relationship between blood pressure and dietary sodium and potassium intake, or the ratio of sodium to potassium intake.

POTASSIUM

Studies and trials show that populations with similar salt intake but different blood pressures had actually different potassium intake, with blacks excreting much less potassium than the white population. As high potassium diet tends to be more expensive, its intake may be a major factor in the epidemiologic differences of hypertension. The first strain of rats bred by Dahl for the trait of "salt sensitivity" demonstrated that incidence of salt-induced hypertension was less when the potassium intake was high.[23]

Years before in 1984, George Daniel Miller, et al in their research showed that there is a slight direct relationship between random urinary sodium concentration and blood pressure and this relationship is more significant for diastolic blood pressure. There exists an inverse relationship between urinary potassium concentration and blood pressure. Dietary sodium to potassium ratio is directly related to the mean blood pressure and is a strong predictor of blood pressure than either of sodium or potassium alone. The relationship between urinary sodium / urinary potassium and blood pressure varies with age, race, and sex.

SODIUM

The daily physiological requirement of sodium for the human body is around 180-230 mg/day. The cation sodium is the most common ion found in the extracellular fluid and it helps to maintain the blood volume, water balance, cell membrane potential, acid-base balance and nerve conduction.

Sodium and its role in the maintenance of blood pressure

There is significant scientific data to suggest that there is a very strong positive association between daily dietary sodium intake and blood pressure within and between populations. Epidemiologic studies have shown that dietary sodium intake is directly proportional to cardiovascular morbidity and mortality and to the rise in blood pressure with aging. Various multi-centric studies regarding the dietary salt intake and blood pressure have demonstrated its adverse prognostic outcome in both hypertensive and non-hypertensive individuals.

Renal Salt Excretion - the need for a proper balance

More than 95% of the dietary salt taken is absorbed from the gastrointestinal tract and the extra-renal loss of salt is insignificant, with normal sweating accounting usually for 0.058 g/d and other extra-renal losses for 0.002 to 0.18 g/d only. After absorption of the dietary salt from the gastrointestinal tract even a minimal increase in serum sodium concentration triggers thirst until the normal serum concentration is restored by taking more fluids. To elaborate, an excess salt intake of 8.3 g must be followed by

1-L increase in water intake to maintain the normal serum sodium concentration.

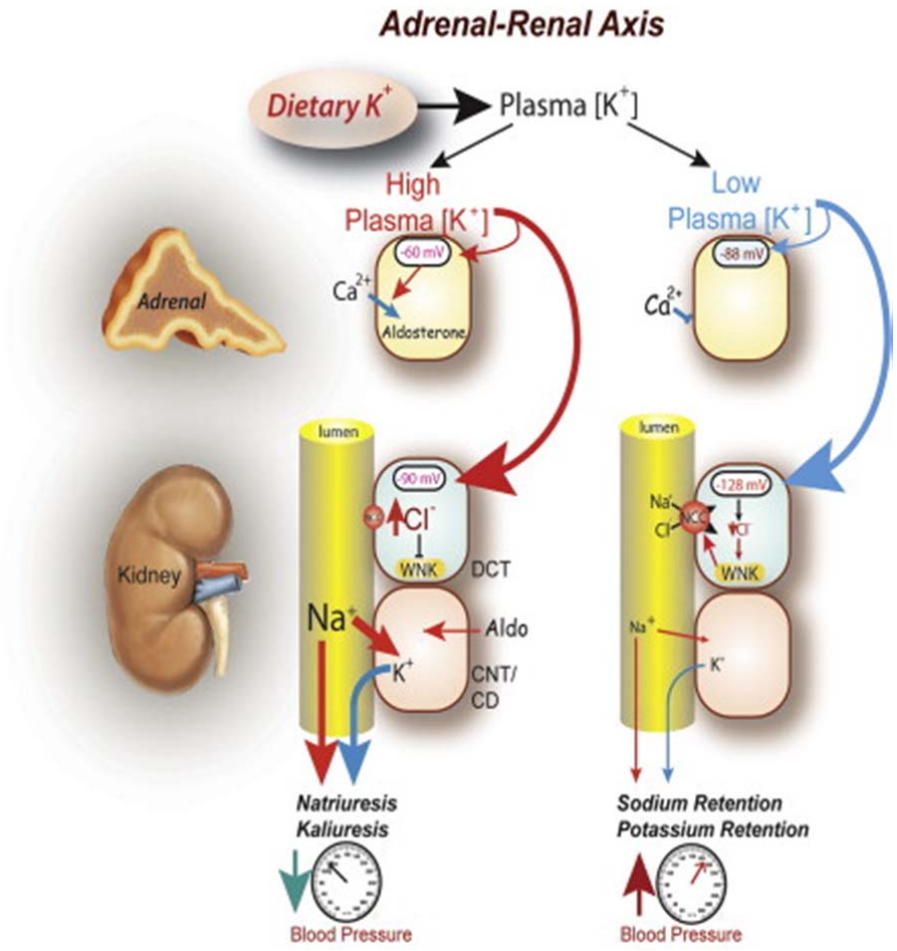


FIGURE 06: Adrenal-Renal axis

Postulated mechanisms of salt-induced hypertension

Since the 1980s, there have been many studies and trials carried out regarding dietary salt intake and blood pressure and yet till date this remains a controversial topic. There are many mechanisms which have been put forth to explain salt- induced hypertension.

Role of Kidneys

Dahl, et al in their scientific experiment with rats showed that when the kidneys of a rat with normal blood pressure is transplanted to another rat with high blood pressures the blood pressure of the recipient rat did not rise and conversely, when the kidneys from a rat with high blood pressure is transplanted to a rat with normal blood pressure, the blood pressure of the recipient rat was elevated. This same phenomenon was obsereved in human population. Adults who were initially known to have systemic hypertension after undergoing a renal transplant (for any cause of chronic kidney disease) from a donor with normal blood pressure, had significant fall in their mean blood pressure values.

Role of extra cellular volume

This is the oldest postulated mechanism for dietary sodium induced hypertension. It is said that the kidneys lose their ability to excrete sodium and hence leading to sodium retention which in turn retain water along with it. This in turn causes plasma volume expansion which initiates other compensatory mechanisms leading to increase in blood pressure which helps the kidneys to excrete sodium.

Role of serum sodium

Recent studies have shown that the daily salt intake causes changes in the serum sodium levels and hence is associated with variations in blood pressure. Many epidemiological studies have proven that there is a positive

association between serum sodium and blood pressure. However the hallmark Framingham Heart Study proved that there was no relation between the serum sodium levels and blood pressure.

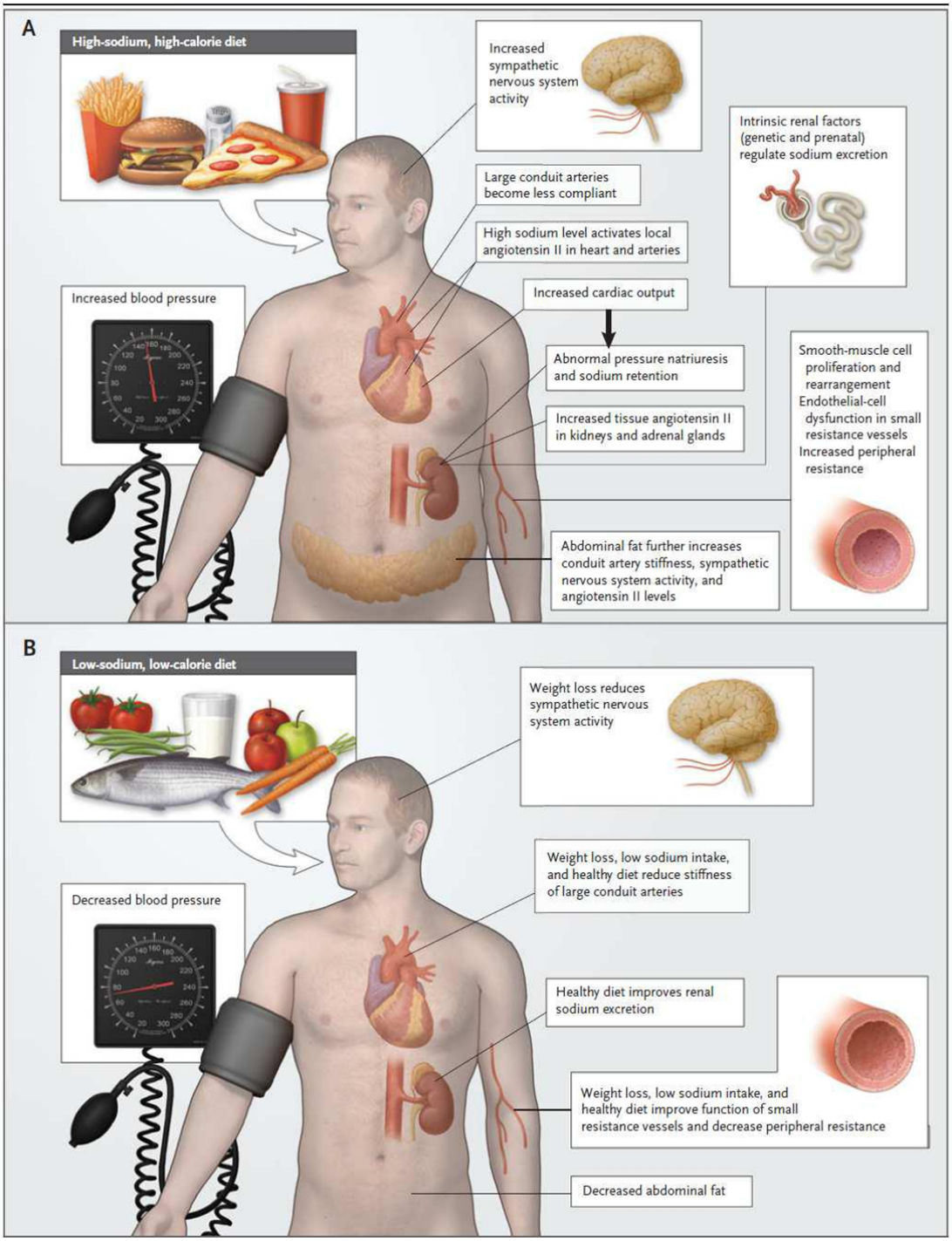


FIGURE 07: Dietary sodium and its association with blood pressure

REVIEW OF RELATED STUDIES

He FJ, Li J, Macgregor G, et al in 2013 did a cochrane based meta-analysis which included 34 trials with 3230 participants. It concluded that even a minimal decrease in the dietary salt intake for 4 or more weeks caused significant fall in blood pressure in both hypertensives as well as non-hypertensives, irrespective of sex and race. This study showed a positive correlation between the decrease in 24-h urinary sodium and the decrease in systolic BP, showing that the more the reduction in dietary salt intake, the greater is the decrease in systolic BP. [21]

Njeri Karanja, Kristie J. Lancaster, et al did a randomized crossover trial among 354 adults with pre-hypertension or stage 1 hypertension in order to study the palatability and compliance of guideline recommendations among hypertensives. They found that the intermediate sodium level was slightly more acceptable than either the higher or lower level especially with the DASH diet. They also found the DASH diet was more acceptable than the control diet at all sodium levels. The study concluded that the lower sodium level-1200 mg/day (current recommendation) as the adequate intake and a goal to aim for, and the intermediate sodium level-2300 mg/day, which is the safe upper limit and well accepted by the participants, should be extrapolated to the population at risk for developing hypertension. [22]

Andrew Mente, Martin J. O'Donnell, Sumathy Rangarajan, et al in 2014 did a multi-centric trial based on the Prospective Urban Rural

Epidemiology (PURE) study which included 102,216 adults from 18 different countries including India. In this study, the association of estimated dietary intake of sodium and potassium which was determined from measurements of urinary excretion of sodium and potassium, with blood pressure was found to be nonlinear and was most significant in persons on high-sodium diet, known hypertensives and elderly population. The Kawasaki formula was used to estimate the 24hr urinary excreted sodium and potassium which was used as a surrogate for the dietary intake of these salts. [23]

Chien, Kuo-Liong, Hsiu-Ching, et al investigated the role of 24-h urinary sodium excretion and its association with hypertension risk among ethnic Chinese. In a prospective community-based cohort study conducted in Taiwan, 1520 middle-aged and elderly participants who were non-hypertensive at baseline were enrolled and was found that high urinary sodium excretion was associated with the risk of developing hypertension. They concluded that urinary sodium excretion could be used as a marker of dietary sodium intake, and can be useful for the evaluation of hypertension risk among the Asian populations.[24]

Minoru Kawamura, Yuki Kusano, et al in 2005 conducted a study in Japan to determine the effectiveness of a Spot Urine Method (SUM) postulated by Kawasaki in evaluating daily salt intake in hypertensive patients taking oral antihypertensive drugs. They estimated the daily salt intake in 73 hypertensive patients by SUM and by a post food consumption

method (FCM) when they were at home, and also by SUM in the hospital with a fixed intake of 7 g of sodium chloride (NaCl). The mean dietary intake at admission in this population was 7-8 gm/day. The study concluded that SUM is a reliable method for evaluating daily salt intake in patients taking antihypertensive medication as well as in patients not on medication and that the Kawasaki formula derived dietary salt intake was significantly related to blood pressure even when applied to post prandial urine sample. [25]

Eberhard Ritz, Nadezda Koleganova,Grzegorz Piecha, et al in 2009 conducted a study in Germany regarding the role of dietary sodium in the progression of Chronic Kideney Disease. They concluded that there was a close relationship between salt intake and the development of hypertension and cardiovascular events, as well as blood pressure−independent target organ damage including kidney disease. Increase in salt causes raised albuminuria in individuals without primary renal disease and increases the excretion of albumin in patients with pre-existing renal disease. It also stated that treatment with diuretics could not replace the effects of dietary salt restriction. [26]

Radhika G, Sathya RM, Mohan V, et al in 2007 did a study among the urban population of South India regarding the dietary salt intake (CURES-53). This study concluded that intake of dietary salt in urban South Indian population is higher than the current WHO recommendation. An increased salt intake was significantly related with increased risk for hypertension. [27]

Deepa R, Premalatha G, Mohan V et al in 2003 conducted the Chennai Urban Population Study (CUPS), an epidemiological study with 1262 participants in Chennai. The study stated that the prevalence of hypertension increased in the presence of other risk factors such as a raised BMI, diabetes, obesity, CAD, PVD, and waist-hip ratio, with the socioeconomic status of the individual playing a major role. [28]

Mohan S, Campbell NR, et al in 2009 evaluated the association between excessive dietary salt intake and the significance of a generalized population-based strategy to decrease the dietary salt and concluded that with the threat of increasing cardiovascular disease all over the world, especially in low economic and developing countries, salt restriction is the most economic strategy to fight hypertension and its associated cardiovascular diseases. [29]

Fodor JG, Whitmore B, Leenen F, et al in 1999 in Canada provided recommendations regarding the effects of salt intake on the prevention and control of hypertension in adults. Salt restriction for the population with normal blood pressure was discouraged. For hypertensives over the age of 44 years, moderate restriction of the dietary intake of sodium 90-130 mmol/day (3-7 g of salt/day) was recommended. The dietary salt was recommended to be estimated by questionnaires. [30]

Burgess E, Lewanczuk R, Bolli P, Chockalingam A, et al in 1999 in Canada provided recommendations on the consumption of potassium, magnesium and calcium. They recommended a daily dietary potassium of

atleast 60 mmol, as it reduced the risk of cerebro vascular accidents. For non-hypertensive people already receiving atleast 60 mmol of potassium in their daily diet supplements were not recommended for prevention of hypertension. In hypertensives already receiving daily dietary potassium of atleast 60 mmol, supplements were not recommended as a treatment. [31]

He FJ, Mac Gregor GA, et al in 2009 made a meta-analysis and concluded that an increased daily salt intake directly increased the risk of strokes, left ventricular hypertrophy and kidney disease independent of its relation with blood pressure. [32]

Park J, Kwock CK, Yang YJ, et al in 2016 investigated the effect of sodium to potassium ratio on blood pressure and the prevalence of hypertension from the Korean National Health and Nutrition Examination Surveys between 2010 and 2014. Higher prevalence rates of hypertension were seen with higher sodium to potassium ratio. [33]

Cook NR, et al in 2008 did a meta-analysis of the association of salt intake with blood pressure and cardiovascular disease among the normal population. It concluded that even with a small change in blood pressure, the cardiovascular disease risk came down by 25% even among the non-hypertensive population. [34]

Huang F, Yu P, Yuan Y, Li Q, et al in 2016 did a study among 951 hypertensive patients and the results suggested that there was a higher level of urinary sodium excretion in the hypertensive population and it was associated with renal and retinal damage. [35]

Sun Yi, Lei Rensheng, Romaina Iqbal, et al in 2016 did a pooled analysis, which studied 133 118 individuals from 49 countries in four large prospective studies and estimated 24-h urinary sodium excretion and equated it to dietary sodium. High sodium intake was associated with an increased risk of cardiovascular events and death among the hypertensives but not in non-hypertensives. It also concluded that there were increased adverse cardiovascular events in normal population taking a low sodium diet. This study implied that measures to reduce the dietary sodium should be targeted to only those with hypertension. [36]

Hooper L, Bartlett C, Davey SG, et al in 2004 did a cochrane review in which there was a follow-up period of up to seven years. They put forth that rigorous measures to restrict sodium intake in the normal population is unwarranted as it produced only a meagre reduction in the blood pressure during long term follow up. [37]

M.J. O'Donnell, A. Mente, A. Smyth, S. Yusuf, et al in 2012 did a met-analysis of eight prospective cohort studies in which two reported a positive association, two reported no association, and four reported a negative association between the dietary salt intake and cardiovascular events. [38]

Suckling RJ, He FJ, Macgregor GA, et al did a meta analysis in 2010 with thirteen studies which showed a significant decrease in blood pressure with dietary salt restriction, almost equivalent to that of individuals on a single antihypertensive drug especially among the non-hypertensives. [39]

Gary Taubes, et al in 1998 did a meta-analysis review which concluded that the apparent benefits of a restricted salt diet were actually biased. It commented that the term called "salt sensitivity" could explain the reason why the blood pressure in some individuals increases with an increased load of dietary salt but not in the entire population. It mocked at the INTERSALT trial which could not justify its hypothesis that there was a positive association between blood pressure and dietary salt intake. [41]

Swales J, et al in 2000 did a meta-analysis and concluded that the reduction of salt intake in non-hypertensives showed very minimal changes of 1 to 2 mm Hg for SBP and 0.1 to 1.0 mm Hg for DBP. It suggested that there were various confounding factors in the trials which showed that there was a significant fall in blood pressure with restricted salt diet. [42]

Fernando Elijovich, Myron H. Weinberger, Cheryl A.M. Anderson, et al in 2016 published a review article which defined salt sensitivity of blood pressure (SSBP) as a physiological trait in humans, wherein few individuals of the population show variations in blood pressure with changes in the amount of dietary salt intake but others do not. This phenomenon is an inbred trait wherein salt-sensitive individuals will exhibit increase in blood pressure with an increased salt diet and decrease with a restricted salt diet, whereas the salt resistant individuals will not show any change. [43]

MATERIALS AND METHODS

Study design: Cross- sectional study

Study setting: General Medicine OPD and General Medicine Ward of Sree Mookambika Institute of Medical Sciences, Kulasekharam

Number of groups to be studied: 2 groups

Detailed description of the groups:

Group A - Non-hypertensives

Group B – Hypertensives (Newly detected, with/without treatment)

Inclusion Criteria :

1. Willing for the study
2. Age – 30 to 80 years
3. Both sex

Exclusion Criteria :

1. Not willing
2. Known cases of secondary hypertension
3. Critically ill
4. Pregnant women and women on OCP

Sample size of each group: 130

Total sample size of the study: 260

Scientific basis of sample size used in the study:

$$N = (1.96)^2 \, pq \, / \, d^2$$

P – Percentage of population with high sodium excretion

P – 43 (Reference 23)

q = 100-p

q = 57

d = 20% of p

d = (20/100) *43 = 8.6

$N = (1.96)^2 * 43 * 57 \, / \, (8.6)^2 = 128$

N = 130 (Rounded off)

Sample size of each group: 130

Total sample size of the study: 130 * 2 = 260

Sampling Technique: Convenience Sampling

Procedure (in brief):

After acceptance of the study by the IHEC, a consent form was kept in the General Medicine OPD and ward. The study was explained to the patient in his/her local language by the principal investigator (myself) and after getting a written informed consent, was enrolled as a participant in this study.

A detailed general physical examination was performed. Basic biochemical investigations and participant information in the form of medical history

(including medication), lifestyle status (diet, exercise, smoking, alcohol status), socioeconomic status, blood pressure, and anthropometric measures (weight, height, waist and hip circumference) were entered in the case record form.

Participant's blood pressure was measured by a mercury sphygmomanometer (Diamond brand). Participants were advised to rest quietly for at least 5 minutes, not to smoke, ingest food or caffeine beverages (coffee, tea or colas), or exercise (including stair climbing) in the previous 30 minutes prior to the time of measurement. In all the cases, blood pressure was recorded by taking 3 readings, while patient was in the sitting position. BP was checked at 15 minutes intervals and the average of the 3 readings was taken as the final value

Each participant was asked to provide a midstream urine sample for analysis. The sample was placed in the sample processing unit and the machine would automatically takeup the sample, process it and provide the result within 5 minutes.

Technique Used : Ion Selective Electrode method

Instrument Used : Beckmann's Coulter 480, fully automatic.

Reagent Used :

Phosphate buffer (pH 6.5) 103 mmol/L,

4 Amino antipyrine 0.31mmol/L.

Phenol 5.2 m mol/L

Cholesterol esterase > 0.2kU/L

Cholesterol oxidase > 0.2kU/L

Peroxidase Preservative > 10kU/L

Kit Used : OSR 6116

Parameters Studied

- Spot Urine Sodium
- Spot Urine Potassium
- Spot Urine Creatinine
- Urine Microalbumin
- Urine Routine
- Fasting blood sugar (mg/dl)
- Post prandial blood sugar (mg/dl)
- HbA1c
- Fasting Lipid Profile
- Triglyceride
- High Density Lipoprotein
- Low Density Lipoprotein
- Very Low Density Lipoprotein
- Serum Urea
- Serum Creatinine
- Serum Uric Acid
- Serum Sodium
- Serum Potassium
- Serum Protein
- Serum Albumin

- Thyroid Stimulating Hormone
- Haemoglobin
- ESR
- ECG
- ECHO

SAMPLE COLLECTION AND METHOD

All the investigations were carried out in the Central Laboratory, Sree Mookambika Institute of Medical Sciences.

Blood sample of not less than 5 ml was collected under aseptic precautions using a sterile disposable syringe.

Urine samples were collected in autoclaved, dry, capped glass bottles. At least 10 ml of random, midstream urine samples were collected from patients.

FIGURE 08 : AU 480 Automated Analyser (Beckman Coulter) Used to measure Sr.Urea , Sr.Creatinine, Sr.Uric acid, Sr.Sodium, Sr.Potassium, Ur.Sodium, Ur.Potassium.

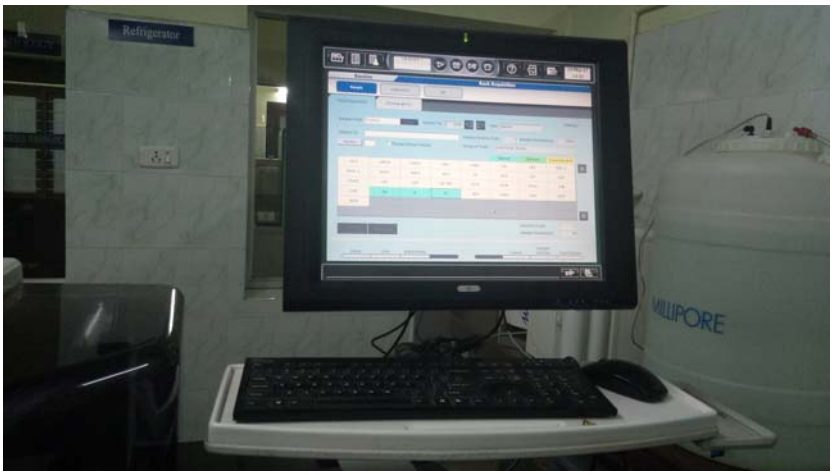


FIGURE 09: AU 480 Automated Analyser Monitor showing the variables for analysis (Beckman Coulter)

FIGURE 10: Unilyte6^{+} Electrolyte Analyzer

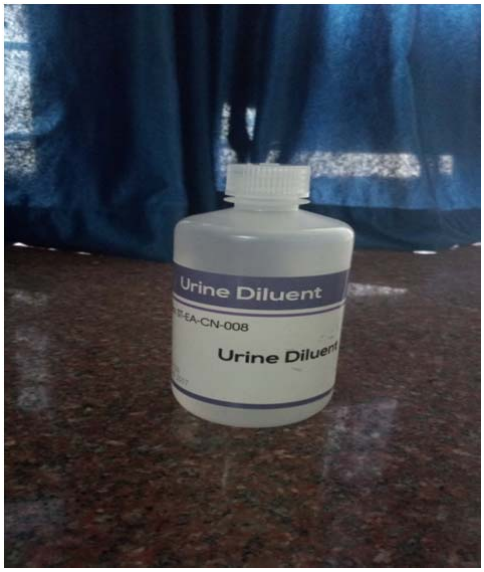


FIGURE 11: Urine Diluent used to dilute urine samples before placing into Unilyte6^{+} Electrolyte Analyzer.

Assessment of urine routine examination for protein:

A sample of uncentrifuged urine, not more than 2 hours old at the time of testing was used by the Strip/Dipstick Method. This is a qualitative semi-quantitative method using Urine Reagent Strips – Urocolor 2 (Biostandard Diagnostics). The reagent coated strips were immersed in the urine sample, removed immediately and compared against the color chart given on the bottle label at 60 seconds after dipping. Depending upon the color chart, the presence of urinary protein is categorized as:

Presence of Urinary Protein	Amount in mg/dl (approx)
Trace	< 30 mg/Dl
(+)	30 – 99 mg/dL
(++)	100 – 299 mg/dL
(+++)	300 – 1999 mg/dL
(++++)	>2000 mg/dL

Table 02: Quantification of amount of urinary protein by Dipstick test

FIGURE 12: Urine Reagent Strips (Dipstick Method)

- **Assessment of serum creatinine:**

  Alkaline picrate method (Modified Jaffe's Method) was used. Blood sample was allowed to clot and the serum was separated. 0.l ml of the same was mixed with 1.0 ml of Reagent R1 and Reagent R2 (manufactured by Beckman Coulter) and quantitative assessment of serum creatinine was obtained after feeding this mixture into the AU 480 automated analyzer (manufactured by Beckman Coulter).

- **Assessment of blood sugar values:**

  Glucose oxidase/peroxidase method was employed. Serum or plasma, free of haemolysis, was used, after mixing with Reagent (manufactured by Beckman Coulter) and analyzed using AU 480 automated analyzer.

FIGURE 13: Reagent R1 and R2 for Assessment of fasting blood sugars

- **Assessment of serum uric acid values:**

  Serum uric acid levels was measured using Uricase Methodology

FIGURE 14: Reagent for serum uric acid

Deriving 24 hour dietary intake of sodium and potassium :

The 24hr urinary excretion of sodium and potassium is directly proportional to the 24 hr dietary intake of sodium and potassium as shown in multiple studies and is used as a surrogate marker as estimating the dietary salt intake by recall methodology or questionnaires was usually biased. [23,24,25]

The 24 hr urinary excretion of sodium is not feasible to be measured as the patient has to be admitted and strict collection principles have to be followed. Thus, measuring 24hr urinary excretion of sodium and potassium for a large scale study becomes impossible. To overcome this hurdle, multiple equations have been formulated and validated.[25,33,38,]

The three widely used equations :

1. KAWASAKI FORMULA

Specimen : 2nd morning urine sample

Predicted 24hr urine creatinine :

Male PrUCr24hr = (15.12*Wt)+(7.39*Ht)-(12.63*Age)-79.9

Female PrUCr24hr = (8.58* Wt)+(5.09*Ht)-(4.72*Age)-74.95

24hr Urinary sodium excretion (mEq/d) :

XNa = (SUNa/SUCr*10)*PrUCr24hr

SUNa = Spot Urine Sodium

SUCr = Spot Urine Creatinine

24hr Urinary sodium excretion (mEq/d) =16.3√ XNa

24hr Urinary sodium excretion (mg/d) = 23 * 24hr Urinary sodium excretion(mEq/d)

24hr Urinary potassium excretion (mEq/d) :

XK = (SUK / SUCr*10)*PrUCr24hr

SUK = Spot Urine Potassium

24hrUK (mEq/d) = 7.2√XK

24hr Urinary potassium excretion (mg/d) = 39*24hrUK (mEq/d)

2. INTERSALT FORMULA

MALE :

23* [(25.46 + 0.468 * SUNa) – 2.75 * SUCr - 0.13 * SUK + 4.10 * BMI + 0.26 * AGE]

FEMALE :

23 * [(5.07 + 0.34 * SUNa) – 2.16 * SUCr – 0.09 * SUK + 2.39 * BMI + 2.35 * AGE – 0.03 * AGE^2]

3. TANAKA FORMULA:

23 * 21098 * (SUNa / SUCr * PrUCr) $^{0.392}$

PrUCr = 14.89 * WEIGHT(kg) + 16.14 * HEIGHT(cm) – 2.04 * AGE ⁻ 2244.45

Among the equations, the Kawasaki formula is the one most widely used in large trials as it takes into account the height , weight and age of the individual and has separate formulas for males and females. [23,24,36]

The Kawasaki formula has been validated for estimating the 24hr urinary sodium and potassium from random urine sample in both hypertensives and non-hypertensives. [23,25]

Hence I have used the Kawasaki formula in the estimation of 24 hour urine sodium and potassium from spot urine samples.

STATISTICAL ANALYSIS:

- Data was entered in Microsoft Excel 2013 spread sheet
- **Significant level decided before starting of study:** $p \leq 0.05$ –95% confidence level
- **Statistical tests to be used for data analysis:** Mean, SD, correlation co-efficient, chi square test, 't' test.
- **Software(s) to be used for the statistical analysis:** SPSS Software Trial Version 20.1

RESULTS AND OBSERVATIONS

SOCIODEMOGRAPHIC CHARACTERS

SEX DISTRIBUTION

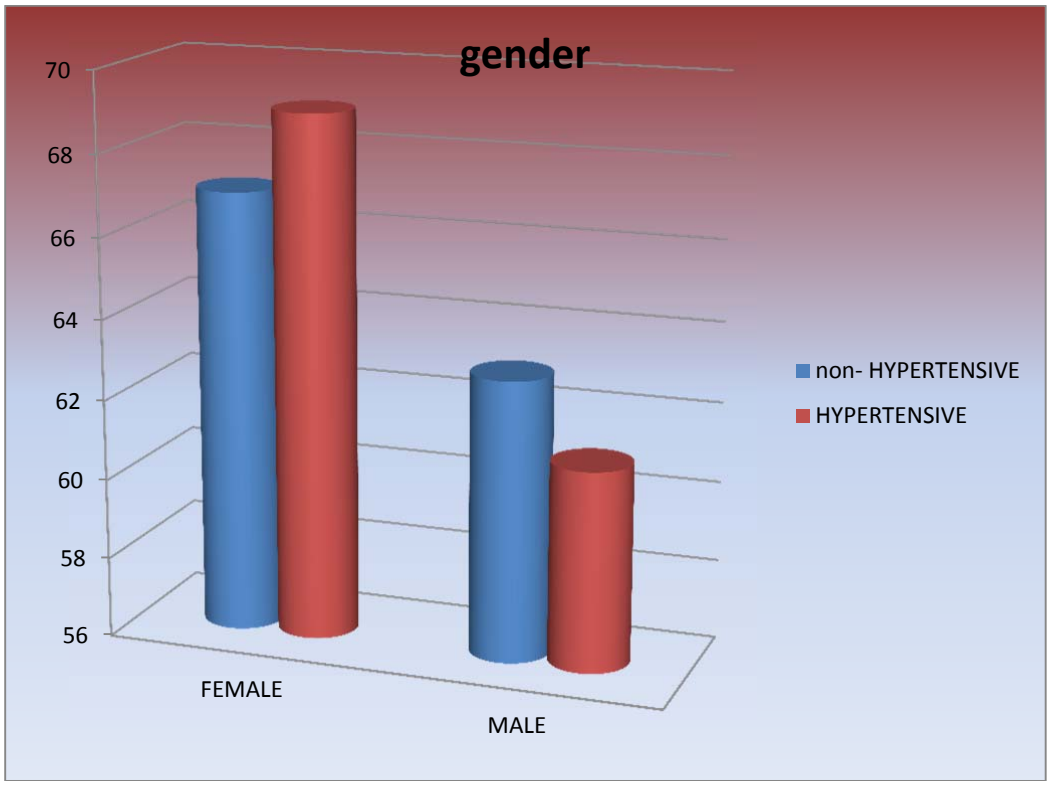
GENDER

NON HYPERTENSIVE	Frequency	Percent
FEMALE	67	51.5
MALE	63	48.5
Total	130	100.0

TABLE 03: Sex distribution among non-hypertensives

HYPERTENSIVE	Frequency	Percent
FEMALE	69	53.1
MALE	61	46.9
Total	130	100.0

TABLE 04: Sex distribution among hypertensives



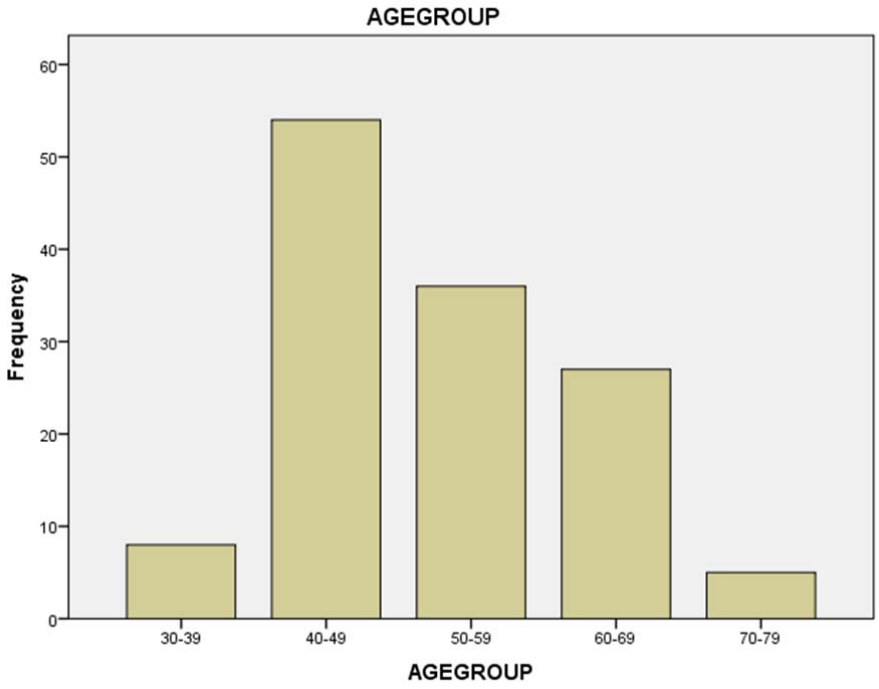
GRAPH 01: Gender comparison among hypertensives and non-hypertensives

The above table and graph show the gender distribution of cases in the study. Most of the cases studied were males. There was no statistically significant difference between the two groups with a p value less than 0.05

AGE DISTRIBUTION-NON HYPERTENSIVE

AGE GROUP	Frequeny	Percent
30-39	8	6.2
40-49	54	41.5
50-59	36	27.7
60-69	27	20.8
70-79	5	3.8
Total	130	100.0

TABLE 05: Age distribution among non-hypertensives



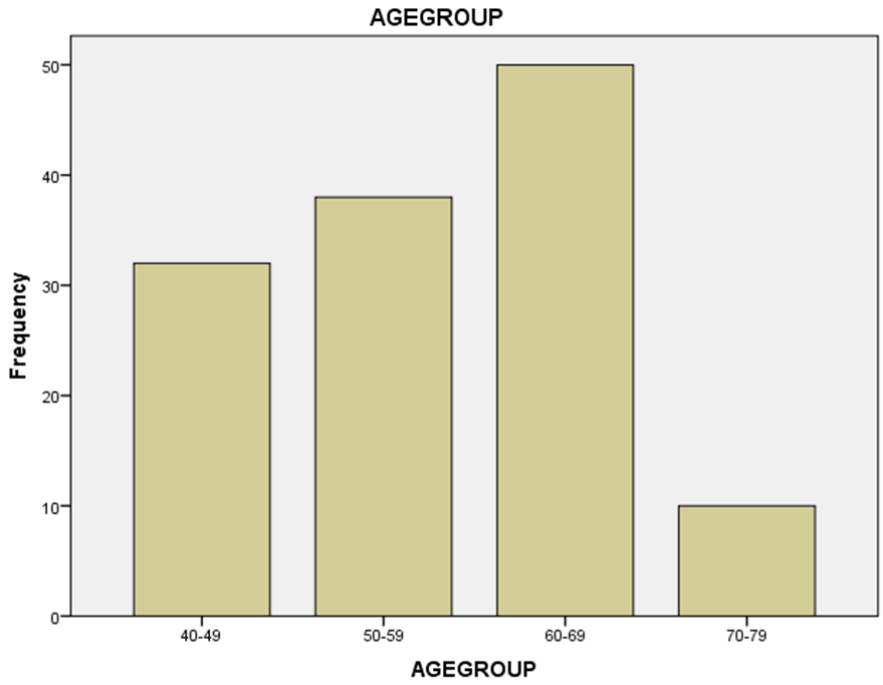
GRAPH 02 : Age distribution among non-hypertensives

The above table and graph show the age distribution of cases in the non-hypertensive group. Most of the cases studied were in the age group 40-49 years among the non-hypertensives.

AGE DISTRIBUTION -HYPERTENSIVE

AGEGROUP	Frequency	Percent
40-49	32	24.6
50-59	38	29.2
60-69	50	38.5
70-79	10	7.7
Total	130	100.0

TABLE 06: Age distribution among hypertensives



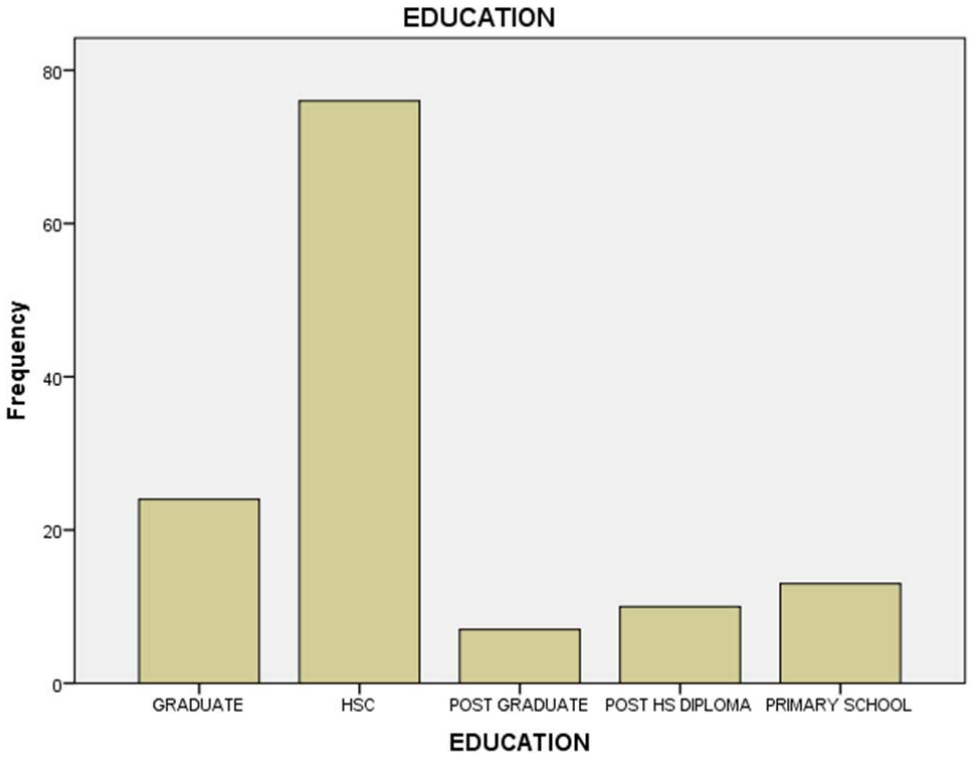
GRAPH 03: Age distribution among hypertensives

The above table and graph show the age distribution of cases in the hypertensive group. Most of the cases were in the age group of 60-69 years. There was statistically significant difference between the two groups with a p value less than 0.05. This shows that as age advances the incidence of hypertension increases.

EDUCATION-NON HYPERTENSIVE

EDUCATION	Frequency	Percent
GRADUATE	24	18.5
HSC	76	58.5
POST GRADUATE	7	5.4
POST HS DIPLOMA	10	7.7
PRIMARY SCHOOL	13	10.0
Total	130	100.0

TABLE 07: Education among non-hypertensives

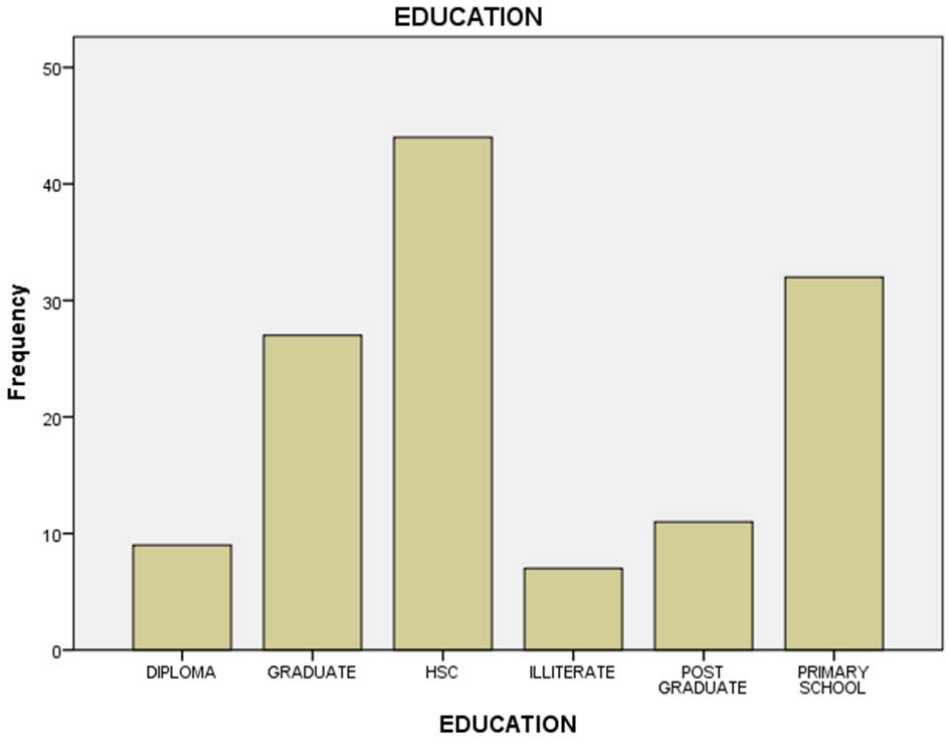


GRAPH 04: Education among non-hypertensives

EDUCATION- HYPERTENSIVE

EDUCATION	Frequency	Percent
DIPLOMA	9	6.9
GRADUATE	27	20.8
HSC	44	33.8
ILLITERATE	7	5.4
POST GRADUATE	11	8.5
PRIMARY SCHOOL	32	24.6
Total	130	100.0

TABLE 08: Education among hypertensives



GRAPH 05: Education among hypertensives

OCCUPATION - NON HYPERTENSIVE

OCCUPATION	Frequency	Percent
CLERICAL	20	15.4
FARMER	8	6.2
PROFESSIONAL	11	8.5
SEMI-PROFESSION	3	2.3
SEMI-SKILLED WORKER	6	4.6
SHOP- OWNER	6	4.6
SKILLED WORKER	26	20.0
UNEMPLOYED	46	35.4
UNSKILLED WORKER	4	3.1
Total	130	100.0

TABLE 09: Occupation among non-hypertensives

GRAPH 06: Occupation among non-hypertensives

OCCUPATION- HYPERTENSIVE

OCCUPATION	Frequency	Percent
CLERICAL	6	4.6
FARMER	5	3.8
PROFESSIONAL	23	17.7
SEMI-PROFESSIONAL	11	8.5
SEMI-SKILLED WORKER	4	3.1
SKILLED WORKER	47	36.2
UNEMPLOYED	34	26.2
Total	130	100.0

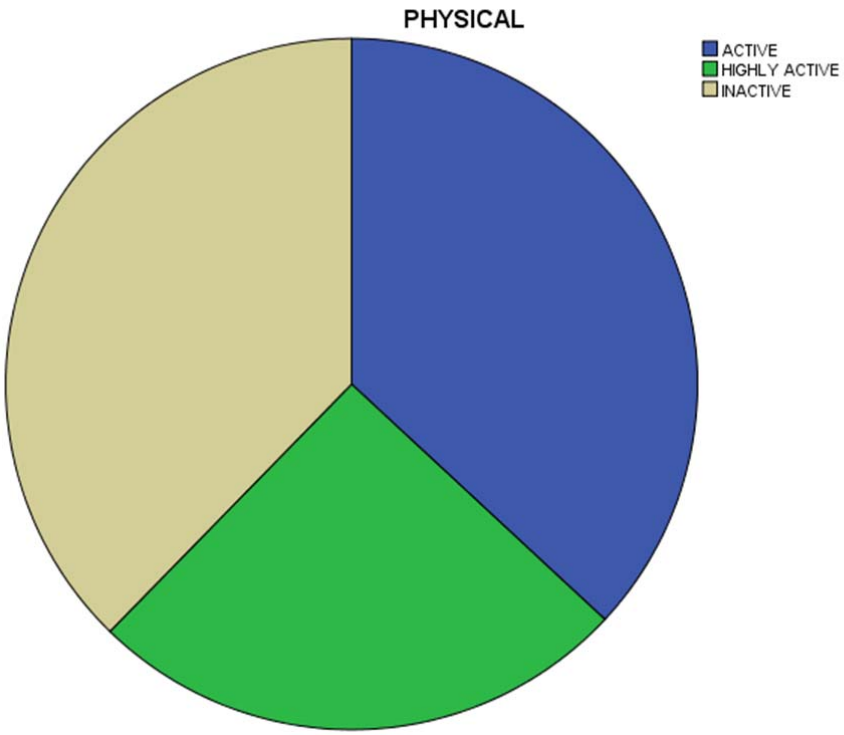
TABLE 10: Occupation among hypertensives

GRAPH 07: Occupation among hypertensives

PERSONAL HABITS
PHYSICAL ACTIVITY -NON HYPERTENSIVE

PHYSICAL	Frequency	Percent
ACTIVE	48	36.9
HIGHLY ACTIVE	33	25.4
INACTIVE	49	37.7
Total	130	100.0

TABLE 11: Physical activity among non-hypertensives



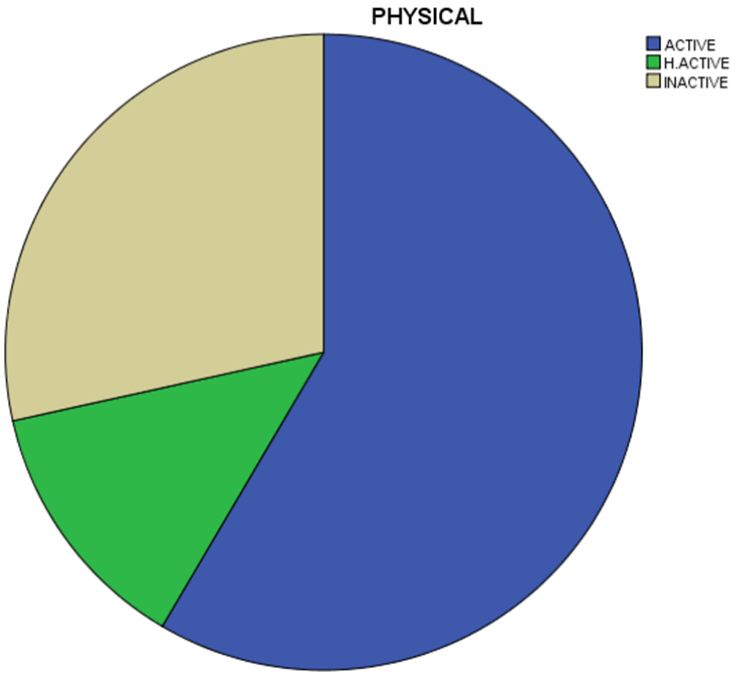
GRAPH 08: Physical activity among non-hypertensives

The above table and graph show the distribution of physical activity in the non-hypertensive group. The inactive cases constituted 37.7% .

PHYSICAL ACTIVITY - HYPERTENSIVE

PHYSICAL	Frequency	Percent
ACTIVE	76	58.5
H.ACTIVE	17	13.1
INACTIVE	37	28.5
Total	130	100.0

TABLE 12: Physical activity among hypertensives



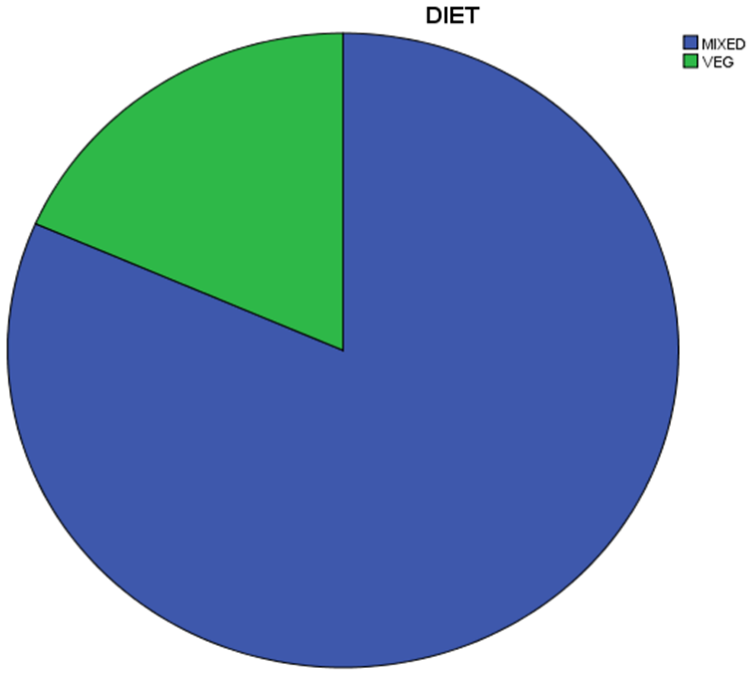
GRAPH 09: Physical activity among hypertensives

The above table and graph show the distribution of physical activity among the cases in the hypertensive group. The inactive cases constituted 28 % of the group.

DIET-NON HYPERTENSIVE

DIET	Frequency	Percent
MIXED	106	81.5
VEG	24	18.5
Total	130	100.0

TABLE 13: Diet among Non-hypertensives



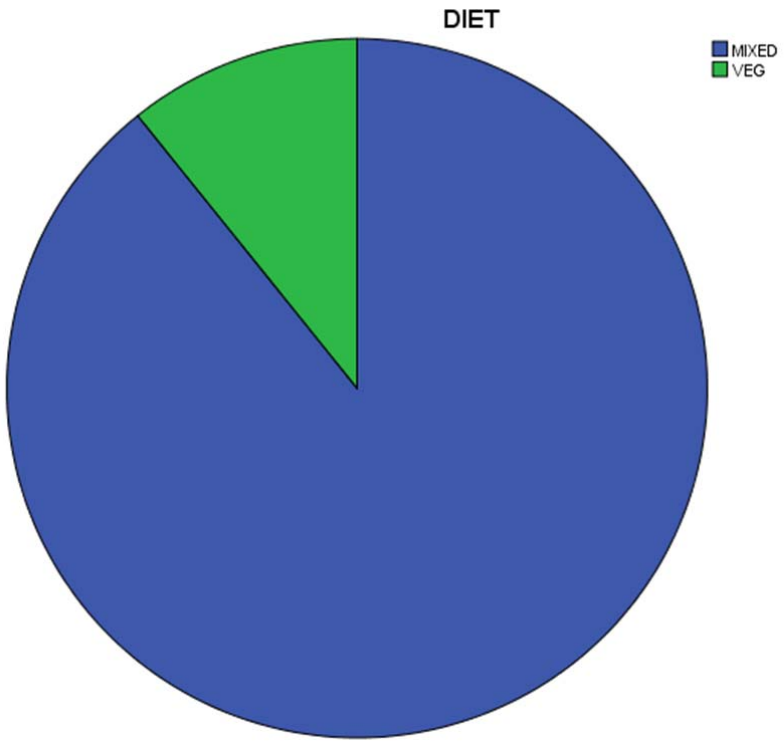
GRAPH 10: Diet among non-hypertensives

The above table and graph show the distribution of dietary habits among the cases in the non hypertensive group. The vegetarians constituted 18.5% of cases.

DIET-HYPERTENSIVE

DIET	Frequency	Percent
MIXED	116	89.2
VEG	14	10.8
Total	130	100.0

TABLE 14: Diet among hypertensives



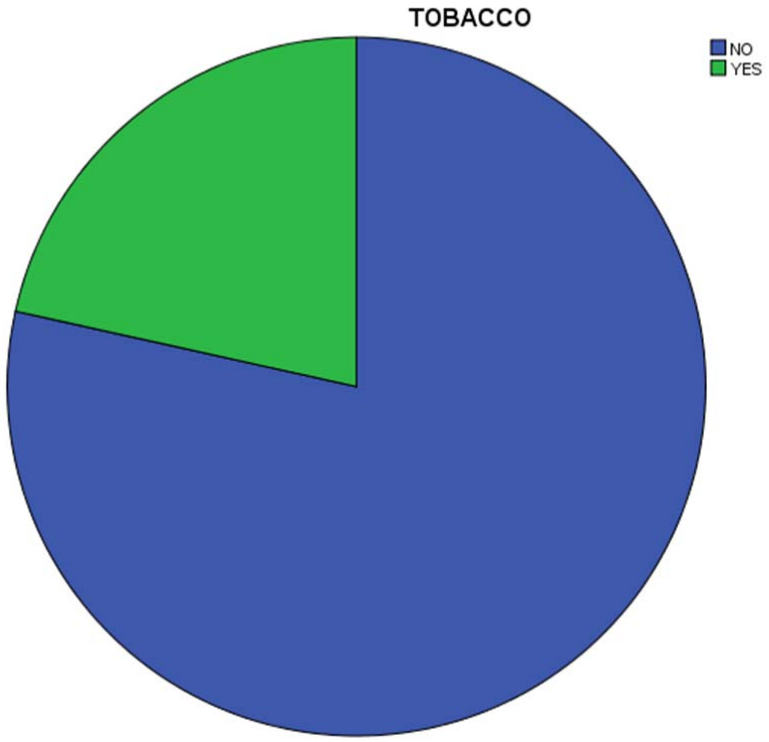
GRAPH 11: Diet among hypertensives

The above table and graph show the distribution of dietary habits among the cases in the hypertensive group. The vegetarians constituted 10.8% of cases

TOBACCO USE-NON HYPERTENSIVE

TOBACCO	Frequency	Percent
NO	102	78.5
YES	28	21.5
Total	130	100.0

TABLE 15: Tobacco use among non-hypertensives



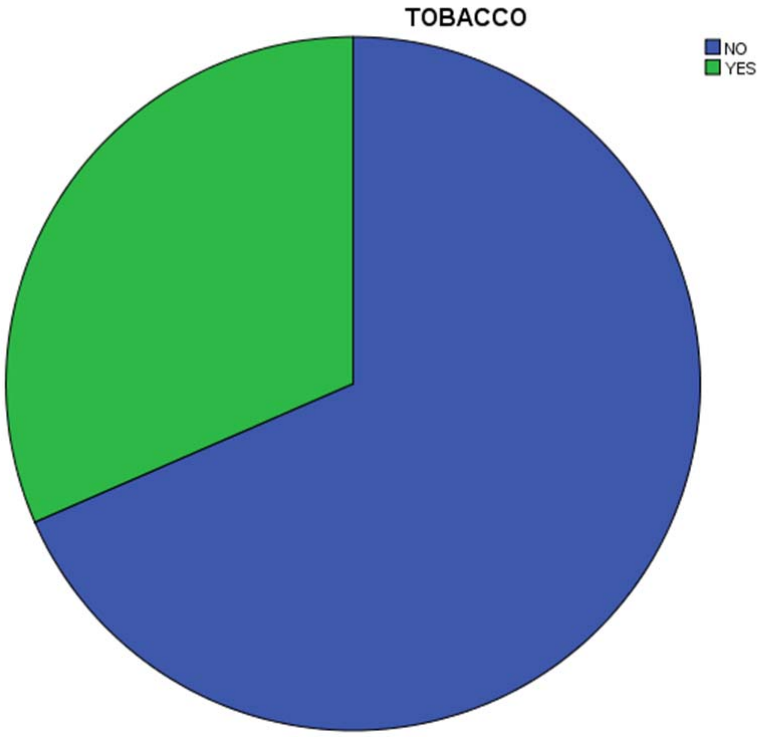
GRAPH 12: Tobacco use among non-hypertensives

TOBACCO USE-HYPERTENSIVE

TOBACCO

TOBACCO	Frequency	Percent
NO	89	68.5
YES	41	31.5
Total	130	100.0

TABLE 16: Tobacco use among hypertensives

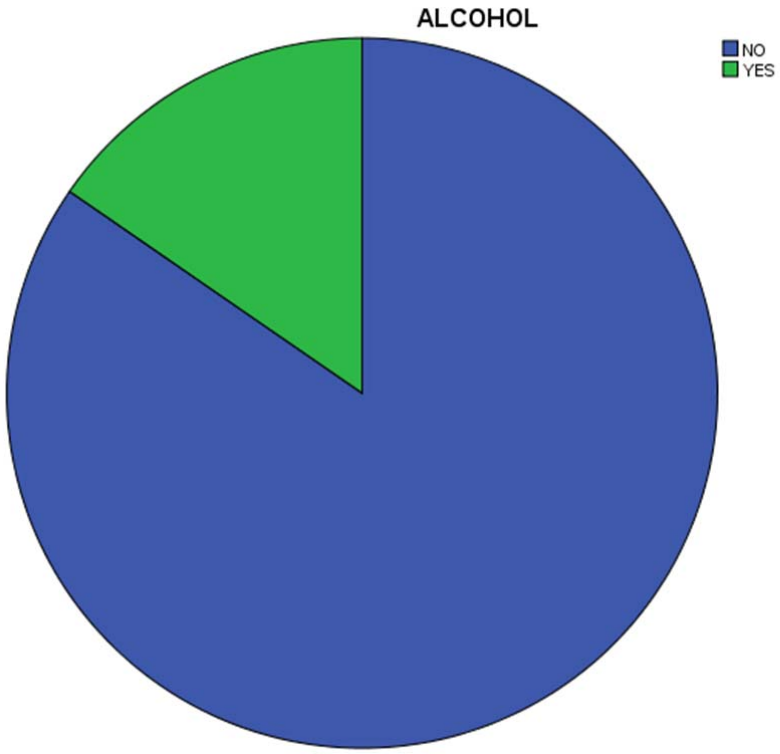


GRAPH 13: Tobacco use among hypertensives

ALCOHOL ABUSE-NON HYPERTENSIVES

ALCOHOL	Frequency	Percent
NO	110	84.6
YES	20	15.4
Total	130	100.0

TABLE 17: Alcohol abuse among non-hypertensives

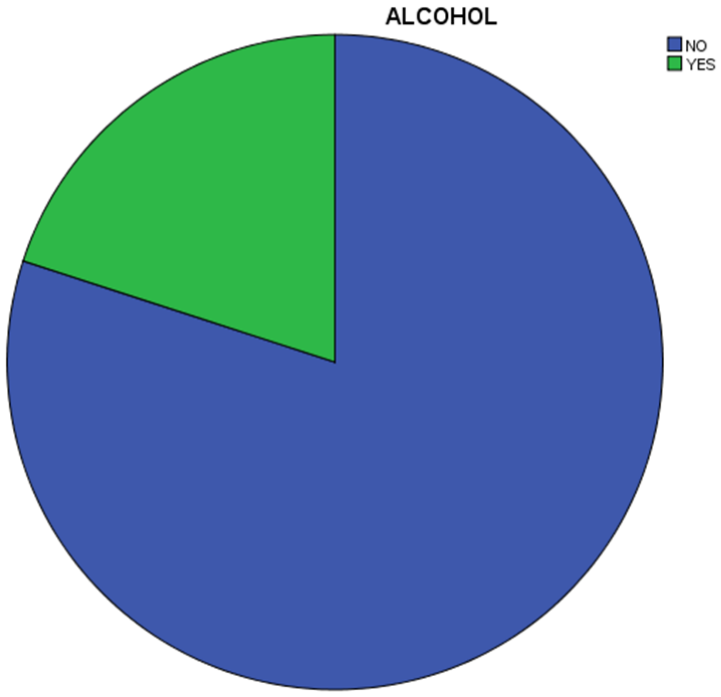


GRAPH 14: Alcohol abuse among non-hypertensives

ALCOHOL ABUSE-HYPERTENSIVE

ALCOHOL	Frequency	Percent
NO	104	80.0
YES	26	20.0
Total	130	100.0

TABLE 15: Alcohol abuse among hypertensives



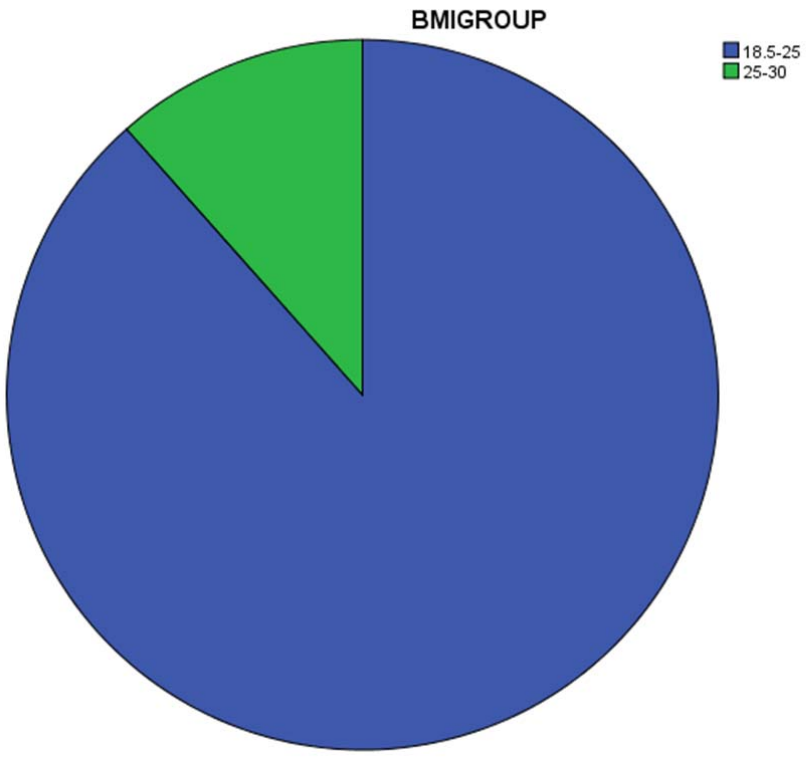
GRAPH 15: Alcohol abuse among hypertensives

GENERAL CHARACTERISTICS

BMI-NON HYPERTENSIVES

BMI	Frequency	Percent
18.5-25	115	88.5
25-30	15	11.5
Total	130	100.0

TABLE 19: BMI of non-hypertensives

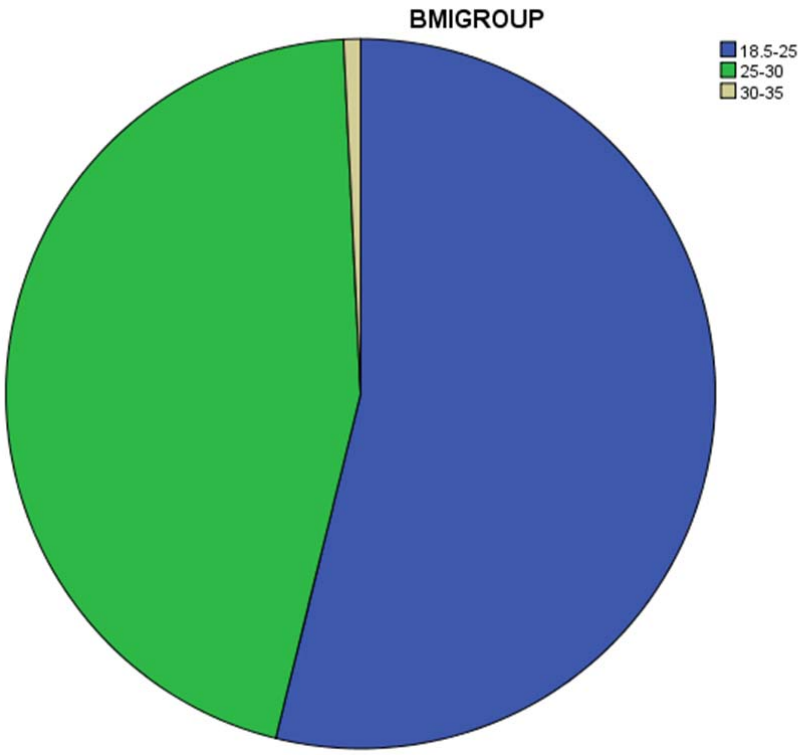


GRAPH 16 : BMI of non-hypertensives

BMI-HYPERTENSIVES

BMIGROUP	Frequency	Percent
18.5-25	70	53.8
25-30	59	45.4
30-35	1	.8
Total	130	100.0

TABLE 20: BMI of hypertensives

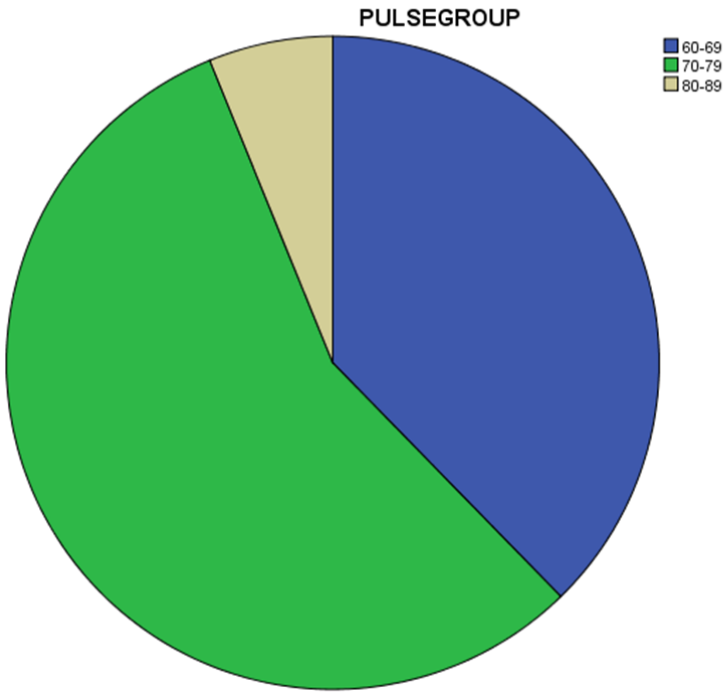


Graph 17: BMI of hypertensives

PULSE RATE-NON HYPERTENSIVE

PULSEGROUP	Frequency	Percent
60-69	49	37.7
70-79	73	56.2
80-89	8	6.2
Total	130	100.0

TABLE 21: Pulse rate among non-hypertensives

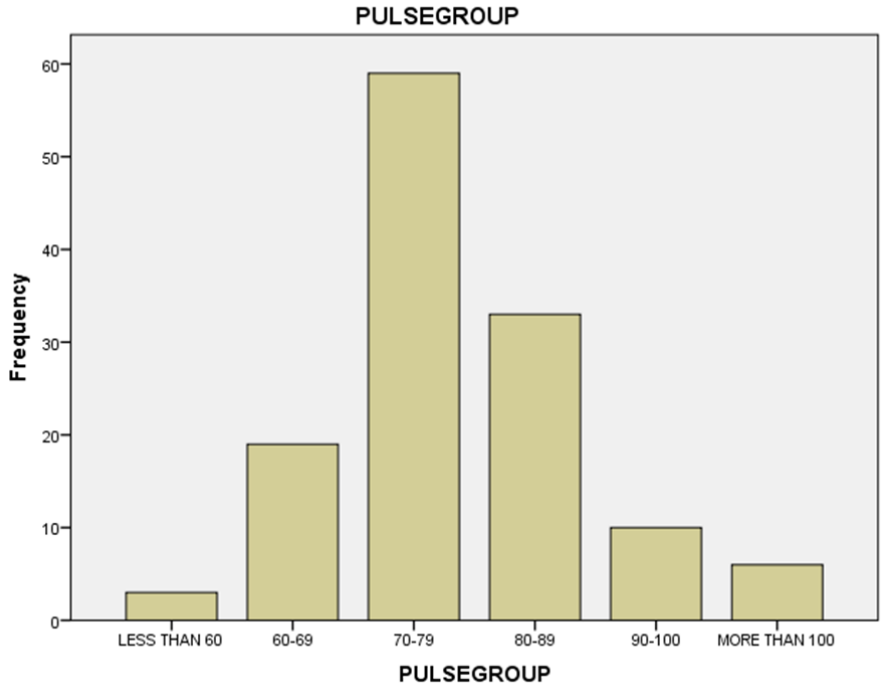


GRAPH 18: Pulse rate among non-hypertensives

PULSE RATE-HYPERTENSIVE

PULSE GROUP	Frequency	Percent
LESS THAN 60	3	2.3
60-69	19	14.6
70-79	59	45.4
80-89	33	25.4
90-100	10	7.7
MORE THAN 100	6	4.6
Total	130	100.0

TABLE 22: Pulse rate among hypertensives



. **GRAPH 19:** Pulse rate among hypertensives

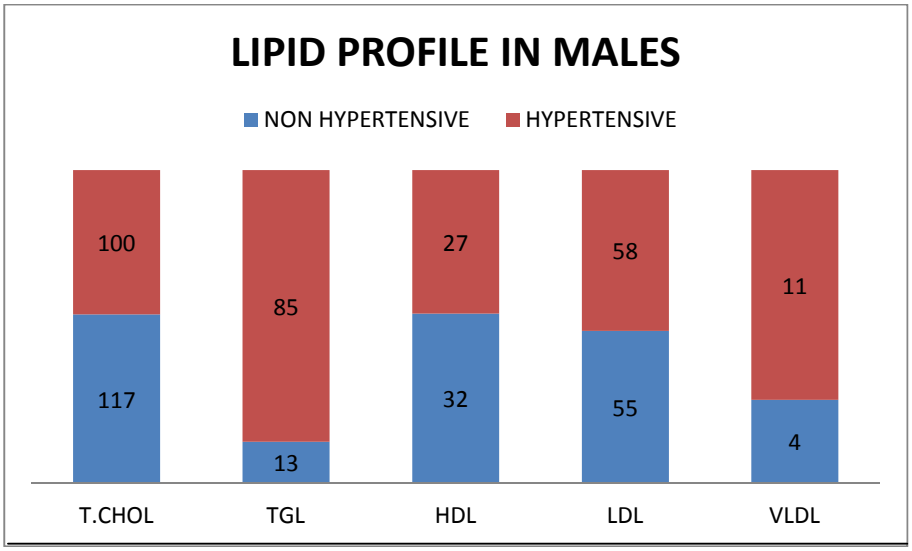
LIPID PROFILE-NON HYPERTENSIVE

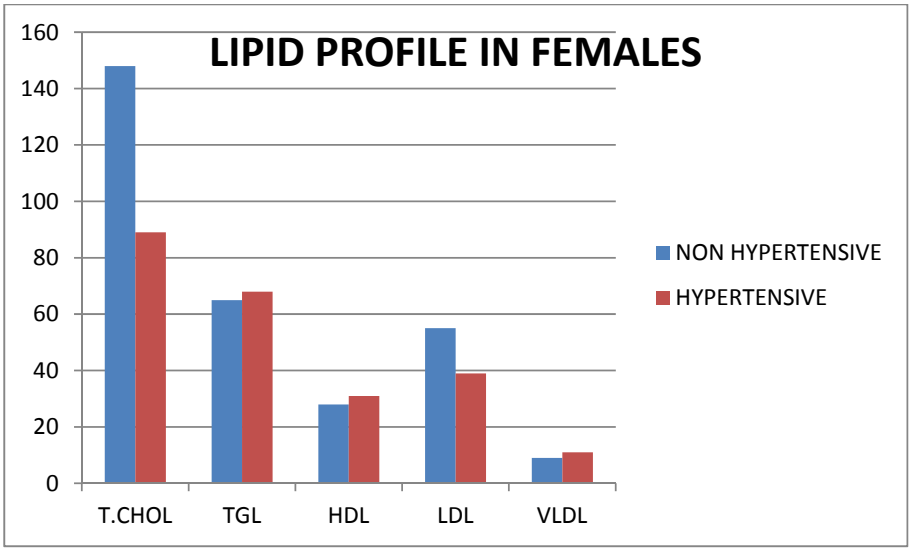
MALE	N	Minimum	Maximum	Mean	Std. Deviation
T.CHOL	63	117	206	176.16	19.230
TGL	63	13	170	120.97	28.240
HDL	63	32	53	39.89	4.701
LDL	63	55	110	85.75	14.383
VLDL	63	4	24	16.51	3.510
FEMALE	N	Minimum	Maximum	Mean	Std. Deviation
T.CHOL	67	148	210	178.99	16.646
TGL	67	65	168	117.04	25.567
HDL	67	28	53	38.52	5.076
LDL	67	55	110	84.25	15.220
VLDL	67	9	27	16.07	3.657

LIPID PROFILE -HYPERTENSIVE

MALE	N	Minimum	Maximum	Mean	Std. Deviation
T.CHOL	61	100	224	173.48	26.172
TGL	61	85	230	131.08	33.233
HDL	61	27	46	37.92	5.502
LDL	61	58	149	107.18	20.033
VLDL	61	11	35	21.33	7.512
FEMALE	N	Minimum	Maximum	Mean	Std. Deviation
T.CHOL	69	89	301	160.81	35.453
TGL	69	68	311	128.28	49.792
HDL	69	31	61	37.61	4.177
LDL	69	39	199	87.65	23.639
VLDL	69	11	62	19.97	10.388

TABLE 23: Lipid profile- Non hypertensive and hypertensive





GRAPH 20: Lipid profile- non hypertensive and hypertensive

GENDER (NON-HYPERTENSIVES)

	FEMALE		MALE	
	SBP	DBP	SBP	DBP
24HrUNa	0.017	-0.086	0.040	0.199
24HrUK	0.159	0.008	0.210	0.093
RATIO	-0.154	-0.083	-0.154	0.044

TABLE 24: Correlation coefficient of SBP, DBP with variables among non-hypertensives

GENDER (HYPERTENSIVES)

	FEMALE		MALE	
	SBP	DBP	SBP	DBP
24HrUNa	-0.132	-0.046	0.348** (0.006)	0.381** (0.002)
24HrUK	0.106	0.179	0.301* (0.018)	0.415** (0.001)
RATIO	-0.329** (0.006)	-0.289* (0.016)	0.302* (0.018)	0.277* (0.031)

TABLE 25: Correlation coefficient of SBP, DBP with variables among hypertensives

CORRELATION (NON-HYPERTENSIVES)

	FEMALE<n=		MALE<n=	
	BMI	W:H RATIO	BMI	W:H RATIO
AGE	0.03	-0.001	0.171	-0.145
BMI	-	0.348**(0.004)	-	0.330**(0.008)
W:H RATIO	0.348**(0.004)	-	0.330**(0.008)	-
SBP	0.018	-0.043	0.064	0.003
DBP	0.027	0.062	0.098	0.115
FBS	-0.052	-0.027	0.042	-0.022
T.CHOLESTEROL	0.040	-0.106	0.020	-0.0288
TGL	0.055	0.059	-0.107	-0.120
HDL	0.052	-0.047	-0.008	-0.141

TABLE 26: Correlation coefficient of BMI, WH Ratio with variables among the non-hypertensives

CORRELATION (HYPERTENSIVES)

	FEMALE		MALE	
	BMI	W:H RATIO	BMI	W:H RATIO
AGE	0.327**(0.006)	0.288*(0.016)	0.359**(0.005)	-0.063
BMI	-	0.419**(0.000)	-	0.178
W:H RATIO	0.419**(0.000)	-	0.178	-
SBP	-0.224	0.017	-0.331**(0.009)	-0.129
DBP	0.047	-0.084	-0.192	0.132
FBS	0.239*(0.048)	0.287*(0.017)	0.211	-0.189
T.CHOLESTEROL	0.099	0.182	0.207	0.228
TGL	-0.132	0.481**(0.000)	0.160	0.303*(0.021)
HDL	0.192	0.083	-0.023	-0.222

TABLE 26: Correlation coefficient of BMI, WH Ratio with variables among the hypertensives

HYPERTENSIVE

	N	Mean	Std. Deviation
BMI	130	25.1536	2.45917
AVG SYS BP	130	147.31	15.086
AVG DIAS BP	130	90.92	7.413
24HrUNa(mg)	130	6343.046876	2362.7289858
24HrUK(mg)	130	2291.613872	534.9343299
24HrUNa/24HrUK (ratio)	130	2.725597	0.5944001

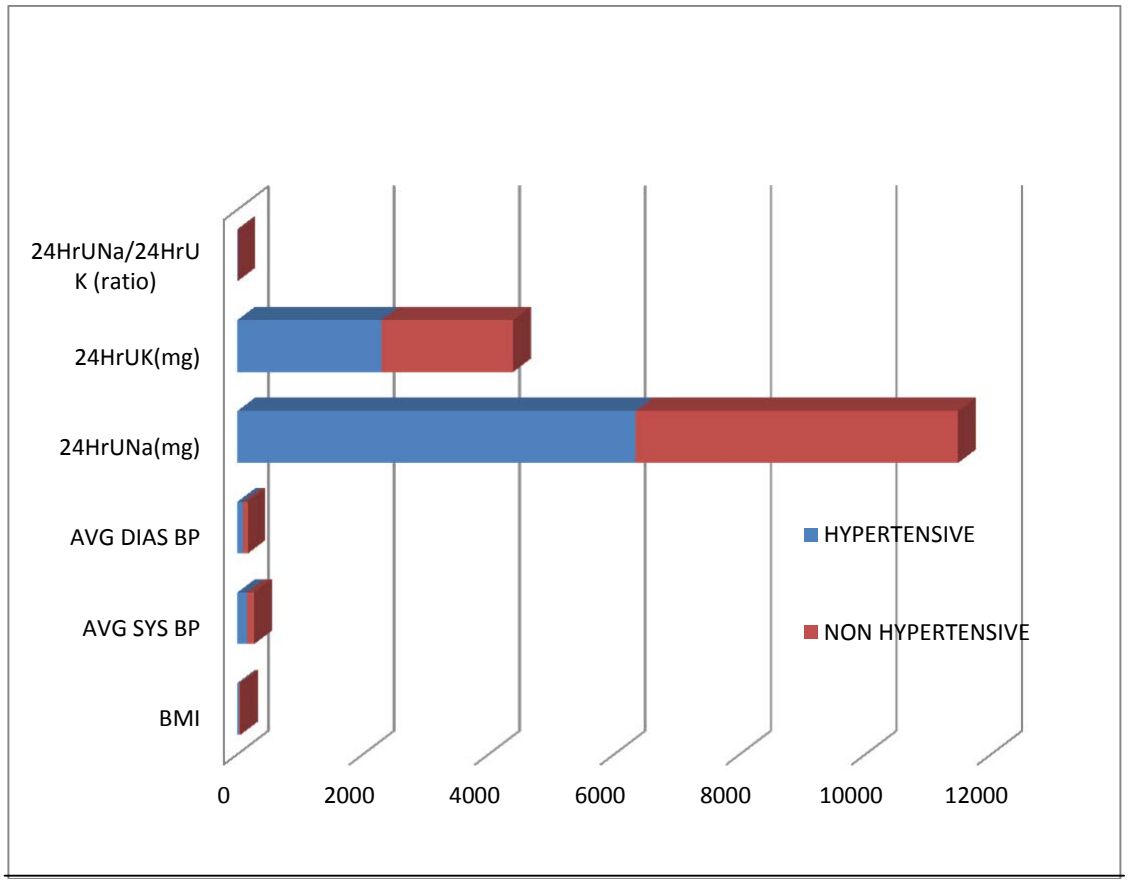
TABLE 28: Comparison of BMI, BP and Urine electrolytes among hypertensives

NON HYPERTENSIVE

Descriptive Statistics

	N	Mean	Std. Deviation
BMI	130	22.7425	2.12617
AVG SYS BP	130	117.62	9.048
AVG DIAS BP	130	72.15	6.931
24HrUNa(mg)	130	5131.489091	1013.6512193
24HrUK(mg)	130	2100.723358	476.4711547
24HrUNa/24HrUK (ratio)	130	2.514944	0.5462737

TABLE 29: Comparison of BMI, BP and Urine electrolytes among non-hypertensives



GRAPH 21: Comparison of BMI, blood pressure and Urine electrolytes among hypertensives and non-hypertensives

Chi-square test is used to find out the association between age, blood pressure with 24 hour urine excretion of sodium (gm) in hypertensive and non-hypertensive patients. p value less than 0.05 is considered as significant.

	(24hrUNa) Non hypertensive		(24hrUNa) Hypertensive	
	Chi square value	p value	Chi square valu	p value
Age	5.764	0.215	16.159	0.013*
SBP	1.330	0.249	9.674	0.046*
DBP	1.039	0.308	24.041	0.000**

(* represents p value less than 0.05, ** represents p value less than 0.01)

TABLE 30: Associaion between age, blood pressure with 24 hour urine excretion of sodium among hypertensives and non-hypertensives

t' test used to compare the mean BMI, systolic blood pressure, diastolic blood pressure, 24 hour urine excretion of sodium, 24 hour urine excretion of potassium, and their ratio between hypertensive and non-hypertensive patients. p value less than 0.05 is considered as significant.

	t-value	p-value
BMI	8.456	0.000**
SBP	19.245	0.000**
DBP	21.087	0.000**
24HrUNa	5.373	0.000**
24HrUK	3.038	0.003**
24HrUNa/24HrUK	2.975	0.003**

TABLE 31: t value comparison

In our study for all variables 'p' values are less than 0.05. So the mean difference of the above variables is significant between hypertensive and non-hypertensive patients (** represents p value less than 0.01).

DISCUSSION

The total number of subjects included in this study was 260. Among these 260 subjects, 130 were hypertensive and 130 were non-hypertensive.

In my study the age of study population varies from 30 to 79 years. Among non hypertensives the maximum frequency of patients were in the range of 40-49yrs whereas among the hypertensives the maximum frequency was in the range of 60-69yrs.

In normotensive group, 51.5% constituted females and 48.5% males. In the hypertensive group 53.1% constituted females and 46.9% males. Hence there was an almost even distribution of sexes in this study population.

The average systolic blood pressure among the non-hypertensives was 117.6 ± 9.05 and average diastolic blood pressure was 72.15 ± 6.93. The average systolic blood pressure among the hypertensives was 143.3 ± 15.1 and average diastolic blood pressure was 90.92 ± 7.41.

In my study, the average urinary sodium excretion in 24 hrs among non-hypertensives was 5131.49 ± 1013.65 mg/d and among hypertensives was 6343.05 ± 2362.73 mg/d.

The average urinary potassium excretion in 24 hrs among the non-hypertensives was 2100.72 ± 476.47 mg/d and among hypertensives was 2291.61 ± 534.93 mg/d.

The mean ratio of 24 hr urinary excretion of sodium to 24 hr urinary excretion of potassium was 2.51 ± 0.55 in the non-hypertensive group and 2.72 ± 0.59 mg/d in the hypertensive group.

Andrew Mente, Martin J.O'Donnell, et al in 2014 conducted the PURE study (Prospective Urban Rural Epidemiology), a multi-centric trial with 102,216 participants from various countries including India. The average 24 hr sodium excretion per day was 4930 ± 1726 mg/d and the average 24 hr potassium excretion per day was 2120 ± 601 mg/d. The average Systolic Bp was 131.7 ± 21.5 mm Hg and the average Diastolic Bp was 81.9 ± 12.2 mm Hg [23]

Park J, Kwock ,et al did a meta analysis in 2016 among the Korean population to find the relation of urinary sodium to potassium ratio with blood pressure .The average daily urine sodium excretion was 4533.17 ± 30.24 mg/d, the average daily urine potassium excretion was 3104.64 ± 15.97 mg/d and the average ratio of daily urine sodium to potassium was 1.54 ± 0.01 [33]

The average daily urine sodium excretion was higher in our study when compared to the other two above mentioned well validated studies possibly indicating the higher dietary salt intake in our

population. It is to be noted that the average daily sodium intake among the non-hypertensives of our population is still higher than the average of the other studies.

Among non-hypertensives, 58.5 % were high school certified whereas in the hypertensive population 33.8% were high school certified. High school certification had the maximum prevalence among both the groups. Education was found to have no significant relation with dietary intake of sodium and potassium in our study.

In my study, among the non-hypertensives 81% of individuals took a mixed diet while 18.5% took a vegetarian diet only while in the hypertensive group 89.2% took a mixed diet and 10.8% a vegetarian diet. No significance was found between blood pressure increase and mixed or vegetarian diet.

The prevalence of tobacco abuse was found to be more among the hypertensives (31.5%) than in the non-hypertensives (21.5%). Alcohol abuse was also found to be more among the hypertensives (20%) when compared to the non hypertensives (15.4%). It is thus observed that the there is a higher prevalence of elevated blood pressures among alcohol and tobacco abusers.

In my study, a statistically significant correlation was seen between the BMI and waist –hip ratio in both males (p-0.008) and

females (p-0.004) in the non hypertensive group and females in the hypertensive group (p-0.000).

In the non hypertensive group, the average BMI was 22.74 ± 2.13 with the majority of individuals in the normal range of BMI (88.5%) with the remaining coming under the overweight category (11.5%). In contrast, among hypertensives the average BMI was 25.15 ± 2.46 with only 53.8% within the normal range and 45.4% in the overweight category and 8% in the obese class I category. Thus it is evident that the prevalence of hypertension is higher with the increasing BMI.

Jay.S.Kaufman, Michael.C.Asuzu, et al in their study which investigated 11,235 adults from Africa concluded that there was a positive correlation between blood pressure and the BMI [45]

Mohan V, Pradeepa R, Premalatha G et al in 2003 in Chennai did an epidemiological study – Chennai Urban Population Study (CUPS) among 1262 individuals. They demonstrated a similar significant relation between BMI, obesity, waist –hip ratio and cardiovascular disease [28]

Among the male hypertensives, there was a significant positive correlation between both systolic Bp (p-0.006) and diastolic Bp (p-0.002) and 24hr urinary sodium. In the same group, there was a significant association of 24 hr urinary excretion of potassium and both

systolic Bp (p-0.018) and diastolic Bp (p-0.001). A positive association was also established between ratio of urinary sodium to potassium to both systolic Bp (p-0.018) and diastolic Bp (p-0.031).

In Andrew Mente, Martin J.O'Donnell,et al trial, they concluded that there was a non-linear association in the excretion of urinary sodium and potassium with blood pressure and was significant especially in individuals known to be hypertensive, elderly population and people binging on high sodium diets [23]

In the Korean study by Kwock CK, et al in 2016, the association of sodium to potassium ratio on blood pressure was evaluated and it stated that higher the urinary sodium to potassium ratio, greater the blood pressure and prevalence of hypertension and its adverse cardiovascular effects [33]

In my study, a statistically significant correlation was seen between the BMI and waist –hip ratio in both males (p-0.008) and females (p-0.004) in the non hypertensive group and females in the hypertensive group (p-0.000).

The chi square test shows a strong association between the 24 hr urinary excretion of sodium (surrogate for 24hr dietary intake of sodium) and systolic (p-0.046) and diastolic (p-0.000) blood pressure in the hypertensive group. A similar association was not seen in the non-hypertensive group.

Leenan F, Whitmore,et al in 1999 in Canada recommended that sodium reduction was not warranted in the individuals with a normal blood pressure and salt restriction of 3-7gm /d was adviced only for the hypertensives [30]

The t-test comparing hypertensives and non hypertensives with other variables showed a significant variation among the hypertensives and non-hypertensives with regard to BMI, systolic Bp, diastolic Bp, 24 hr Urine sodium, 24 hr Urine potassium and the ratio of daily Urine sodium to potassium. These results are similar to the Chennai Urban Population Study (CUPS) by Shanthirani CS, et al [28]

The estimated daily dietary intake of sodium and potassium was high in both the hypertensives and non-hypertensives when compared to other studies.[23,33] There was a positive correlation between the daily urinary sodium and potassium and its ratio with both systolic and diastolic Bp among the hypertensives. The daily urine sodium and potassium had no significant association with blood pressure in the non-hypertensives. Thus, the alternate hypothesis of this study is scientifically proved to be true.

CONCLUSION

- There is a positive association between 24hr urine sodium and potassium (surrogate for 24 hr dietary sodium and potassium) and both systolic and diastolic blood pressure among hypertensives.

- There is a significant relation between ratio of 24hr urine sodium to potassium and both systolic and diastolic blood pressure among the hypertensives.

- The estimated daily dietary intake of sodium and potassium in our study is higher in both the hypertensives and non-hypertensives when compared to various other studies.

- There is a statistically significant positive correlation between BMI and Waist – Hip ratio among both males and females in the normotensives.

- Dietary salt reduction should be recommended to all hypertensives to reduce the risk of further cardiovascular complications.

LIMITATIONS

- The dietary sodium and potassium values obtained are estimated and not measured.
- All biochemical tests were carried out only once and hence day to day variability could not be accounted.
- When compared to other studies the sample size was small.
- Being a hospital based study, the participants may not represent the actual picture in the general population.

SUMMARY

Lifestyle changes and daily stress have lead to the increase in the global incidence of hypertension. Among the non-communicable diseases, cardiovascular morbidity and mortality holds the major proportion which is attributed to the increase in incidence of hypertension. Restricting dietary salt has emerged as one of the major modifiable risk factors in the control of hypertension. Estimating the dietary intake of salt is thus important to the clinician in order to further manage the individual regarding his/her blood pressure control, modification in the dietary allowance, stratifying the risk of further developing cardiovascular and other complications and its optimal management.

The study was a hospital based cross sectional study conducted in Sree Mookambika Institute of Medical Sciences, Kulasekharam, KanyaKumari district.

The total number of subjects included in this study was 260. Among those 260 subjects, 130 were hypertensive and 130 were non-hypertensive. In my study the age of study population varies from 30 to 79 years. In the non-hypertensive group, 51.5% constituted females and 48.5% males. In the hypertensive group, 53.1% constituted females and 46.9 % males. Hence there was an almost even distribution of sexes in this study population.

The average systolic blood pressure among the non-hypertensives was 117.6 ± 9.05 and average diastolic blood pressure was 72.15 ± 6.93. The average systolic blood pressure among the hypertensives was 143.3 ± 15.1 and average diastolic blood pressure was 90.92 ± 7.41.

The average urinary sodium excretion in 24 hrs among non-hypertensives was 5131.49 ± 1013.65 mg/d and among hypertensives was 6343.05 ± 2362.73 mg/d. The average urinary potassium excretion in 24 hrs among the non-hypertensives was 2100.72 ± 476.47 mg/d and among hypertensives was 2291.61 ± 534.93 mg/d. The mean ratio of 24 hr urinary excretion of sodium to 24 hr urinary excretion of potassium was 2.51 ± 0.55 in the non-hypertensive group and 2.72 ± 0.59 mg/d in the hypertensive group.

The average daily urine sodium excretion was higher in our study when compared to other large scale studies possibly indicating the higher dietary salt intake in our population . It is noted that the average daily sodium intake among even the non-hypertensives of our population is still higher than the average of other studies.

The prevalence of tobacco abuse was found to be more among the hypertensives (31.5%) than in the non-hypertensives (21.5%). Alcohol abuse was also found to be more among the hypertensives (20%) when compared to the non-hypertensives(15.4%). It is thus observed that the there is a higher prevalence of elevated blood pressures among alcohol and tobacco abusers.

A statistically significant correlation was seen between the BMI and waist –hip ratio in both males and females in the non-hypertensive group and females in the hypertensive group.

In the non-hypertensive group, the average BMI was 22.74 ± 2.13 with the majority of individuals in the normal range of BMI (88.5%) and others in the overweight category (11.5%). Among hypertensives, the average BMI was 25.15 ± 2.46 with only 53.8% within the normal range and 45.4% in the overweight category and 8% in the obese class I category. Thus it is evident that the prevalence of hypertension is higher with increasing BMI. A significant correlation was seen between the BMI and waist –hip ratio in both males and females in the non hypertensive group and females in the hypertensive group.

Among the male hypertensives, there was a significant positive correlation between both systolic Bp and diastolic Bp and 24hr urinary sodium, 24 hr urinary excretion of potassium and ratio of 24 hr urinary sodium to potassium. A strong association was seen between the 24 hr urinary excretion of sodium (surrogate for 24hr dietary intake of sodium) and systolic and diastolic blood pressure in the hypertensive group. A similar association was not seen in the non-hypertensive group.

When comparing hypertensives and non-hypertensives with other variables a significant variation was seen with regard to BMI, systolic Bp,

diastolic Bp, 24 hr Urine sodium, 24 hr Urine potassium and the ratio of daily Urine sodium to potassium.

The estimated daily dietary intake of sodium and potassium was high in both the hypertensives and non-hypertensives when compared to other studies. There was a positive correlation between the daily urinary sodium and potassium and its ratio with both systolic and diastolic Bp among the hypertensives. The daily urine sodium and potassium had no significant association with blood pressure in the non-hypertensives.

The high prevalence of cardiovascular diseases and their early incidence in our population could well be attributed to the high salt diet in our society. Large scale randomized controlled trials are necessary to followup these patients to understand the safe and permissible levels of daily salt intake in our diet. Urinary sodium and potassium and their ratio in particular could well be developed into a risk stratification tool to screen patients thereby preventing and delaying if not stopping the pandemic of hypertension and its cardiovascular morbity and mortality.

BIBLIOGRAPHY

1. Cowley AW Jr, Nadeau JH, Baccarelli A,et al.Report of the National Heart, Lung, and Blood Institute Working Group on epigenetics and hypertension. Hypertension. 2012;59:899-905.

2. Available at http://www.who.int/gho/ncd/mortality_morbidity/ ncd_ total_ text/ en/index .html. Last accessed on 12.12.12.

3. Anand SS, Yusuf S. Stemming the global tsunami of cardiovascular disease. Lancet 2011;377:529-532.

4. JAPI • FEBRUARY 2013 • VOL. 61 INDIAN GUIDELINES ON HYPERTENSION- 111 2013

5. Indian Guidelines Management of Hypertension 2001. Hypertension India 2001;15:1-34.

6. MeissnerI, Whisnant JP, Sheps S, Schwartz G, O'Fallon WM, Coralt J, et al. Stroke prevention: assessment of risk in a community: the SPARC study, part 1: blood pressure trends, treatment and control (abstract). Ann Neurol 1997;42:433.

7. Brown RD Jr, Whitsnant JP, Sicks JD, O'Fallon WM, Wiebers D. Stroke incidence, prevalence and survival: Secular trends in Rochester, Minnesota, through 1989. Stroke 1996;27:373-380.

8. Vasan RS, Larson MG, Leip EP, Evans JC, O'Donnell CJ, Kannel WB, et al . Impact of high-normal BP on the risk of cardiovascular disease. New Engl J Med 2001;345:1291-1297.

9. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens 2004;18:73-78.

10. National Programme for Prevention and Control of Cancer,Diabetes, Cardiovascular diseases and Stroke (NPCDCS) Operational Guidelines. Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India.

11. Teo K et al; PURE Investigators-Writing Group.The Prospective Urban Rural Epidemiology (PURE) study: examining the impact of societal influences on chronic noncommunicable diseases in low-, middle-, and high-income countries.Am Heart J 2009;158:1-7.e1.

12. Gupta R et al. Obesity is major determinant of coronary risk factors in India: Jaipur Heart Watch studies. Indian Heart J 2008;60:26-33

13. World Health Organisation. Report of tha Joint WHO/FAO Expert Consultation. Diet, Nutrition and the prevention of chronic diseases. Geneva: World Health Organisation; 2003. (WHO Technical Report Series, No 916).

14. Hu HH, Sheng WY, Chu FL, Lan CF, Chiang BN ,et al.Incidence of stroke in Taiwan. Stroke 1992;23:1237-1241.doi:10.1161/01.STR.23.9.1237

15. Tuomilehto J, Jousilahti P, Rastenyte D, Moltchanov V, et al. Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study. Lancet 2001;357:848-851

16. He J, Ogden LG, Vupputuri S, Bazzano LA, et al. Dietary sodium intake and subsequentrisk of cardiovascular disease inoverweight adults. JAMA 1999; 282:2027-2034

17. Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med2001;344:3-10. doi:10.1056/NEJM200101043440101.

18. Whelton PK, Kumanyika SK, Cook NR, et al. 18.Efficacy of nonpharmacologic interventions in adults with high-normal blood pressure: results from phase 1 of the Trials of Hypertension Prevention. Trials of Hypertension Prevention Collaborative Research Group. Am J Clin Nutr 1997;65(2 Suppl):652S-660S.

19. Whelton PK, Appel LJ, Espeland MA,et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. JAMA 1998;279:839-846.

20. He FJ, MacGregor GA , et al. Effect of modest salt reduction on blood pressure: a meta-analysis of randomized trials. Implications for public health. J Hum Hypertens 2002;16:761-770. doi:10.1038/sj.jhh.1001459.

21. **He FJ**, **Li J**, Macgregor GA,et al. Effect of longer-term modest salt reduction on blood pressure **BMJ.** 2013 Apr 3;346:f1325.

22. Njeri Karanja,Kristie J. Lancaster, Eva Obarzanek, et al. Acceptability of Sodium-Reduced Research Diets, Including the Dietary Approaches to Stop Hypertension Diet, among Adults with Prehypertension and Stage 1 Hypertension Published in J Am Diet 2011 Nov 17.

23. Andrew Mente, Ph.D., Martin J. O'Donnell, M.B., Ph.D., Sumathy Rangarajan, et al. Association of Urinary Sodium and Potassium Excretion with Blood Pressure The NEJM August 14, 2014 Vol. 371 No. 7

24. Chien, Kuo-Liong[a,b]; Hsu, Hsiu-Ching[b]; Chen, Pei-Chun[c]; et al. Urinary sodium and potassium excretion and risk of hypertension in Chinese: report from a community-based cohort study in Taiwan Journal of Hypertension:**September 2008 - Volume 26 - Issue 9 - p 1750–1756** doi: 10.1097/HJH. 0b013e 328306a0a7

25. Minoru Kawamura, Yuki Kusano, Toru Takahashi, Masahiko Owada and Takashi Sugawara, et al. Effectiveness of a Spot Urine Method in Evaluating Daily Salt Intake in Hypertensive Patients Taking Oral Antihypertensive Drugs Hypertension Research (2006) 29, 397–402; doi:10.1291/hypres.29.397

26. Eberhard Ritz MD ,Nadezda Koleganova, MD,Grzegorz Piecha, MD

Department of Internal Medicine, Ruperto Carola University, Heidelberg, Germany Role of Sodium Intake in the Progression of Chronic Kidney Disease Journal of Renal Nutrition Jan 2009 Vol.19

27. **Radhika G**, **Sathya RM**, **Sudha V**, **Ganesan A**, **Mohan V**. Dietary salt intake and hypertension in an urban south Indian population[CURES - 53]JAPI 2007 Jun;55:405-11

28. **Shanthirani CS**, **Pradeepa R**, **Deepa R**, **Premalatha G**, **Mohan V** et al.Prevalence and risk factors of hypertension in a selected South Indian population-the Chennai Urban Population Study JAPI 2003 Jan;51:20-7

29. **Mohan S**, **Campbell N**. Salt and high blood pressure.**Clin SciLond.** 2009 Jun 2;117(1):1-11

30. **Fodor JG**, **Whitmore B**, **Leenen F**, **Larochelle P**. Lifestyle modifications to prevent and control hypertension.Canadian Hypertension Society.**CMAJ.** 1999 May 4;160(9 Suppl):S29-34.

31. **Burgess E**, **Lewanczuk R**, **Bolli P**, **Chockalingam A**, **Cutler H**, **Taylor G**Lifestyle modifications to prevent and control hypertension. Recommendations on potassium, magnesium and calcium.**CMAJ.** 1999 May 4;160(9 Suppl):S35-45.

32. **He FJ**, **MacGregor GA**A comprehensive review on salt and health and current experience of worldwide salt reduction programmes.**J Hum Hypertens.** 2009 Jun;23(6):363-84.

33. **Park J**[1], **Kwock CK**[2], **Yang YJ**[3]. The Effect of the Sodium to Potassium Ratio on Hypertension Prevalence: A Propensity Score Matching Approach. **Nutrients.** 2016 Aug 6;8(8). pii: E482. doi: 10.3390/nu8080482.

34. **Cook NR** Salt intake, blood pressure and clinical outcomes.**Curr Opin Nephrol Hypertens.** 2008 May;17(3):310-4.

35. **Huang F**, **Yu P**, **Yuan Y**, **Li Q**, et al. The relationship between sodium excretion and blood pressure, urine albumin, central retinal arteriolar equivalent.**BMC Cardiovasc Disord.** 2016 Oct 11;16(1):194.

36. **Sun Yi**, **Lei Rensheng**, **Romaina Iqbal**, et al.Association of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies The Lancet DOI: **http://dx.doi.org/10.1016/S0140-6736(16)30467-6**

37. **Hooper L**, **Bartlett C**, **Davey SG**, **Ebrahim S**. Advice to reduce dietary salt for prevention of cardiovascular disease.**Cochrane Database Syst Rev.** 2004; (1):CD003656.

38.M.J. O'Donnell, A. Mente, A. Smyth, S. Yusuf Salt intake and cardiovascular disease: why are the data inconsistent? Eurheartjournal DOI: **http://dx.doi.org/10.1093/eurheartj/ehs409** 1034-1040

39. **Suckling RJ**, **He FJ**, **Macgregor GA**. Altered dietary salt intake for preventing and treating diabetic kidney disease.**Cochrane Database Syst Rev.** 2010 Dec 8;(12):CD006763.

40. **Graudal NA**, **Galloe AM**, **Garred P**. Effects of sodium restriction on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride: a meta-analysis. **JAMA.** 1998 May 6;279(17):1383-91.

41. Gary Taubes The (Political) Science of Salt .Science 14 Aug 1998:Vol. 281, Issue 5379, pp. 898-907

42. **Swales J**. Population advice on salt restriction: the social issues. **Am J Hypertens.** 2000 Jan;13 (1 Pt 1):2-7.

43. Fernando Elijovich, Myron H. Weinberger, Cheryl A.M. Anderson,et al.Salt Sensitivity of Blood Pressure A Scientific Statement From the American Heart AssociationHypertension.
2016;68:e7-e46

44. www.ajmc.com/journals/.../the-jnc-8-hypertension-guidelines-an-in-depth-guide

45. Jay.S.Kaufman, Michael.C.Asuza, Jacob.M.Hypertension 1997:30:1511:1516

46. Dahl LK, Thompson K, Heine M. Genetic Influence of Renal Homografts on Blood-Pressure of Rats from Different Strains. Proceedings of the Society for Experimental Biology and Medicine 1972;140(3):852-&.

47. Dahl LK, Heine M, Thompson K. Genetic Influence of Kidneys on BloodPressure - Evidence from Chronic Renal Homografts in Rats with Opposite Predispositions to Hypertension. Circulation Research 1974;34(1):94-101. (88) Curtis JJ, Luke RG, Dustan HP, Kashgarian M, Whelchel JD, Jones

48. ESC Guidelines committee.J Hypertens 2003;21:1011-5

49. J Clin Hypertens (Greenwich). 2009;11:358–368.

ANNEXURE – I

INSTITUTIONAL HUMAN ETHICS COMMITTEE

SREE MOOKAMBIKA INSTITUTE OF MEDICAL SCIENCES,
KULASEKHARAM, TAMILNADU

Communication of Decision of the Institutional Human Ethics Committee(IHEC)

SMIMS/IHEC No: 1 /Protocol no: 36 / 2016

Protocol title: ASSOCIATION OF DIETARY SODIUM AND POTASSIUM WITH BLOOD PRESSURE IN A TERTIARY CARE CENTRE
Principal Investigator: Dr. Shahbaz Zailu Mohamed
Name& Address of Institution: Department of General Medicine Sree Mookambika Institute of Medical Sciences, Kulasekharam ☑ New review ☐ Revised review ☐ Expedited review
Date of review (D/M/Y): 15.12.2016 Date of previous review , if revised application:
Decision of the IHEC: ☑ Recommended ☐ Recommended with suggestions ☐ Revision ☐ Rejected
Suggestions/ Reasons/ Remarks:
Recommended for a period of :two months

Please note*

- Inform IHEC immediately in case of any Adverse events and Serious adverse events.
- Inform IHEC in case of any change of study procedure, site and investigator
- This permission is only for period mentioned above. Annual report to be submitted to IHEC.
- Members of IHEC have right to monitor the trial with prior intimation.

Reneegalyangadhar

Signature of Member Secretary IHEC

SREE MOOKAMBIKA INSTITUTE OF MEDICAL SCIENCES * KULASEKHARAM *
IHEC
Date 21/12/16

ANNEXURE - II

LIST OF ABBREVIATIONS USED

HbA_1c	-	Glycosylated haemoglobin
DM	-	Diabetes Mellitus
BMI	-	Body mass index
VLDL	-	Very low density lipoprotein
HDL	-	High density lipoprotein
LDL	-	Low density lipoprotein
FBS	-	Fasting blood sugar
PPBS	-	Post Prandial blood sugar
RBS	-	Random blood sugar
UA	-	Uric acid
JNC	-	Joint National Committee
SBP	-	Systolic Blood Pressure
DBP	-	Diastolic blood pressure
HTN	-	Hypertension
YRS	-	Years
SUM	-	Spot Urine Method
FCM	-	Food Consumption Method
SUNa	-	Spot Urine Sodium
SUK	-	Spot Urine Potassium

SUCr	-	Spot Urine Creatinine
CV	-	Cardio Vascular
ESH	-	European Society of Hypertension
ESC	-	European Society of Cardiology
ACC	-	American College of Cardiology
AHA	-	American Heart Association
ASH	-	American Society of Hypertension
ADA	-	American Diabetic Association
CDA	-	Canadian Diabetic Association
ISH	-	International Society of Hypertension
TOD	-	Target Organ Damage
ACC	-	Accompanying Clinical Condition
DASH	-	Dietary Approaches to Stop Hypertension
NaCl	-	Sodium Chloride
CURES	-	Chennai Urban Rural Epidemiology Study

ANNEXURE - III

CONSENT FORM

PART 1 OF 2

INFORMATION FOR PARTICIPANTS OF THE STUDY

Dear Volunteers,

We welcome you and thank you for your keen interest in participating in this research project. Before you participate in this study, it is important for you to understand why this research is being carried out. This form will provide you all the relevant details of this research. It will explain the nature, the purpose, the benefits, the risks, the discomfort, the precautions and the information about how this project will be carried out. It is important that you can read and understand the contents of the form carefully. This form may contain certain scientific terms and hence, if you have any doubts or if you want more information, you are to ask the study personnel or the contact person mentioned below before you give your consent and also at any time during the entire course of the project.

1.	**Name of the Principal Investigator:**	Dr. Shahbaz Zailu M Postgraduate – M.D General Medicine Sree Mookambika Institute of Medical Sciences, Kulasekharam
2.	**Name of the Guide:**	Dr. R.Mohandhas Professor Department of General Medicine SreeMookambika Institute of Medical Sciences, Kulasekharam
3.	**Name of Co-guide:**	Dr. V. Rajendran Professor Department of General Medicine SreeMookambika Institute of Medical Sciences, Kulasekharam
4.	**Institute: details with Address:**	SreeMookambika Institute of Medical Sciences, Kulasekharam Kanyakumari District Tamil Nadu-629161

5. Title of the study:

ASSOCIATION OF DIETARY SODIUM AND POTASSIUM WITH BLOOD PRESSURE IN A TERTIARY CARE CENTRE

6. Background Information:

Hypertension is today's number one silent killer all over the world. Hypertension is reported to be the fourth contributor to premature death in developed countries and the seventh in developing countries

There is a continuous relationship between the level of blood pressure and the risk of CV complications. Starting at 115/75 mmHg, CVD risk doubles with each increment of 20/10 mm Hg throughout the blood pressure range. There is evidence that the risk of cardiovascular events in Asian Indians is higher at relatively lower levels of blood pressure.

The prevalence of hypertension in the last six decades has increased from 2% to 25% among urban adults and from 2% to 15% among the rural adults in India and the prevalence rates of coronary artery disease and stroke have more than tripled. Hypertension awareness, treatment and control status in our country is low. It has been seen that only one in five persons is on treatment and less than 5% are controlled. Preventive measures are required so as to reduce obesity, increasing physical activity, decreasing the salt intake of the population and a concerted effort to promote awareness about hypertension and related risk behaviors.

Effective population-based interventions are required to reduce the global burden of cardiovascular disease (CVD). Reducing salt intake has emerged as a leading target, with many guidelines including the World Heart Organization (WHO) in 2003, recommending that adults ingest <2.0 g/day of sodium (which corresponds to 5 g of salt/day). However, there have been a number of studies that have questioned whether the recommended target of sodium intake is optimal, with some recent studies reporting that intakes of under 3 g/day may be associated with an increased risk of CV death.

Thus, despite a large number of studies evaluating the association between sodium intake and blood pressure and CVD there remains a controversy surrounding the optimal target for dietary sodium intake.

7. Aims and Objectives:

To find out the association of dietary intake of sodium and potassium as estimated from the urinary excretion of these cations and their relation with blood pressure.

8. Scientific Justification of the study:

In this era of modern medicine, NCDs form the major cause of morbidity and mortality. The largest proportion of NCD deaths is caused by cardiovascular diseases. Over the years, studies have shown a continuous linear relationship between high sodium intake and the risk of cardiovascular disease. These results are yet insufficient to conclude whether low sodium intake is associated with an increased or reduced risk of cardiovascular disease in the general population.

Recently, few studies have also shown that a low salt intake may be associated with adverse health effects in some subgroups, especially patients with heart failure or other forms of cardiovascular disease, diabetes, or chronic kidney disease. Thus, there are inconsistencies whether a low sodium diet decreases the CV risk among the normal population and hypertensives or in the contrary is actually deleterious.

The association of dietary sodium and potassium with blood pressure is thus a very interesting and controversial topic. There are very few Indian studies from Chennai regarding the subject. The dietary intake of sodium and potassium and its relation to blood pressure and other parameters among the population visiting our tertiary care centre SMIMS, Kulasekharam would make a good study.

In this dissertation, I have proposed to estimate the dietary intake of sodium and potassium from the urinary excretion of these cations and compare it with the blood pressure of normotensives and hypertensives .

9. Procedure of the study:

After acceptance of the study by the IHEC, a consent form will be kept in the General Medicine OPD and ward. The study would be explained to the patient in his/her local language by the principal investigator and after getting a written informed consent, would be enrolled as a participant in this study.

A detailed general physical examination would be performed.Basic biochemical investigations and participant information in the form of medical history (including medication), lifestyle status (diet, exercise, smoking status), socioeconomic status, blood pressure, and anthropometric measures (weight, height, waist and hip circumference) would be entered in the case record form.

Participant's blood pressure would be measured by a mercury sphygmomanometer. Participants would be advised to rest quietly for at least 5 minutes, not to smoke, ingest food or caffeine beverages (coffee, tea or colas), or exercise (including stair climbing) in the previous 30 minutes prior to the time of measurement.

Each participant will provide one midstream urine samples for analysis. The sample would be placed in the sample processing unit and the machine will automatically take this sample, process it and provide the result within 5 minutes.

10. Expected risk of the participants: No risk

11. Expected Benefits of the Research for the participants:

To decrease the risk of cardiovascular and other comorbidities and mortality by intensive counseling and dietary modification and thereby intervening a modifiable risk factor - blood pressure.

12. **Maintenance of confidentiality:** All data collected for the study will be kept confidentially and would reflect on general statistical evaluation only and would not reveal any personal details

13. **Why have I been chosen to be in this study:** You fulfil the criteria of selection

14. How many people will be in the study: 260

15. Agreement of compensation to the participants: No

16. **Anticipated prorated payment, if any, to the participants of the study:** Nil

17. **Can I withdraw from study at any time during the study period:** Yes

18. **If there is any new finding/information, would I be informed:** Yes

19. **Expected duration of the participants participation in the study:** One visit

20. Any other pertinent information: No

21. Whom do I contact for further information: Dr. Shahbaz Zailu M

For any study related queries, you are free to contact

Dr. Shahbaz Zailu M
Post Graduate – M.D General Medicine
Department of General Medicine
Sree Mookambika Institute of Medical Sciences,
Kulasekharam
Mobile number: 00091 8281027768
e-mail: shahbaz.zailu@gmail.com

Place:

Date:

Signature of Principal Investigator

Signatre of Participant

CONSENT FORM

PART 2 OF 2

TITLE OF THE PROJECT: Association of dietary sodium and potassium with blood pressure in a tertiary care centre

PARTICIPANTS NAME:

ADDRESS:

The details of the study have been provided to me in writing and explained to me in my own language. I confirm that I understood the above study and had the opportunity to ask questions, I understand that my participation in this study is voluntary and that I am free to withdraw at any time. Withdraw at any time, without giving any reason, without the medical care that will be normally be provided by the hospital being affected. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose. I have been given an information sheet giving details of this study. I fully consent to participate in the above study.

(I also consent/ do not consent to use my stored biological samples for future scientific purposes: Yes/No – if Applicable)

Signature of the Participant: _____ Date:_____

Signature of Witness:_____ Date:_____

Name and Address of Witness:

Signature of the Investigator:_____ Date: _____

ANNEXURE - IV

ASSOCIATION OF DIETARY SODIUM AND POTASSIUM WITH BLOOD PRESSURE IN A TERTIARY CARE CENTRE

PROFORMA

PARTICIPANT NUMBER :

GROUP A NON HYPERTENSIVE __

GROUP B HYPERTENSIVE __ (KNOWN / NEWLY DETECTED)

OP/ IP NUMBER :

NAME :

AGE : GENDER :

EDUCATION STATUS :

OCCUPATION :

FAMILY INCOME PER MONTH :

LEVEL OF PHYSICAL ACTIVITY :

INACTIVE/ LOW

ACTIVE

HIGHLY ACTIVE

TOBACCO USE

NEVER / FORMER / CURRENT

PACK YEARS: _____

ALCOHOL CONSUMPTION

NEVER / FORMER / CURRENT

DIET

MEDICATION H/O PAST 1 MONTH :

FAMILY HISTORY :

CO MORBIDITIES: DURATION MEDICATION

1.HYPERTENSION`

2.DIABETES MELLITUS

3.DYSLIPIDEMIA

4.CORONARY ARTERY DISEASE

5.CONGESTIVE HEART FAILURE

6.CEREBROVASCULAR ACCIDENT

7.PERIPH OBSTR VASCULAR DISEASE

ANTHROPOMETRY

WEIGHT _____ kg

HEIGHT _____ cm BMI _____ kg/m^2

WAIST CIRCUMFERENCE ____ cm

HIP CIRCUMFERENCE ____ cm WHR _____

BLOOD PRESSURE

SUPINE _____ mm Hg

SITTING _____mm Hg

STANDING _____mm Hg

PLUSE SUPINE _____ /min

SITTING _____/min

STANDING _____/min

CLINICAL EXAMINATION

PALLOR : ICTERUS :

CYANOSIS : CLUBBING :

LYMPHNODE ENLARGEMENT : PEDAL EDEMA :

JVP : RENAL BRUIT :

CVS :

RS :

P/A :

CNS :

LABORATORY DATA

HAEMOGLOBIN :

ESR :

FASTING LIPID PROFILE

TOTAL CHOLESTEROL : HDL :

TRIGLYCERIDE : VLDL :

LDL :

FASTING BLOOD SUGAR (FBS) :

POST PRANDIAL BLOOD SUGAR (PPBS) :

HBA1C :

SERUM UREA :

SERUM CREATININE :

SERUM URIC ACID :

SERUM SODIUM :

SERUM POTASSIUM :

SERUM PROTEIN :

SERUM ALBUMIN :

URINE ROUTINE

ALBUMIN	:	PUS CELLS	:
SUGAR	:	BACTERIA	:
RBC	:	CASTS	:

URINE

SODIUM :

URINE POTASSIUM :

URINE CREATININE :

URINE MICROALBUMINURIA :

TSH :

ECG :

ECHO :